

Devi, S.  
08/905293

08/905293

=> fil reg; d que l1; fil caplu; d que l5

FILE 'REGISTRY' ENTERED AT 16:24:14 ON 07 DEC 1998  
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Key terms

L1 3645 SEA FILE=REGISTRY ABB=ON PLU=ON IMMUNOGLOBULIN ?/CN

FILE 'CAPLUS' ENTERED AT 16:24:15 ON 07 DEC 1998  
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FILE COVERS 1967 - 7 Dec 1998 VOL 129 ISS 24  
FILE LAST UPDATED: 7 Dec 1998 (981207/ED)

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

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all substance data from the REGISTRY file. Enter HELP FIRST for  
more information.

L1 3645 SEA FILE=REGISTRY ABB=ON PLU=ON IMMUNOGLOBULIN ?/CN  
L2 75102 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR IMMUNOGLOBULIN OR  
IMMUNO GLOBULIN OR IG  
L3 218 SEA FILE=CAPLUS ABB=ON PLU=ON L2(S) TOXIC?  
L4 25 SEA FILE=CAPLUS ABB=ON PLU=ON L3(S) INHIBIT?  
L5 4 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND (LEX OR LEY OR LE  
OR BR96 OR (BR OR CHIBR OR HBR) (W) 96 OR CHIBR96 OR HBR96  
OR HB10460 OR HB10036 OR HB(W) (10460 OR 10036) OR MOAB  
Searcher : Shears 308-4994

08/905293

OR MAB OR MONOCLON?)

=> d 1-4 .bevstr

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1998 ACS

AN 1998:112463 CAPLUS

DN 128:204075

TI A method for **inhibiting immunoglobulin-induced toxicity** resulting from the use of **immunoglobulins** in therapy and in vivo diagnosis

IN Rosok, Mae Joanne; Yelton, Dale E.

PA Bristol-Myers Squibb Co., USA

SO PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 9805787	A1	19980212	WO 97-US13562	19970801
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9739688	A1	19980225	AU 97-39688	19970801
PRAI	US 96-23033		19960802		
	WO 97-US13562		19970801		

AB The present invention provides a method for **inhibiting Ig-induced toxicity** resulting from immunotherapy in a subject comprising administering an **Ig** or **Ig** fusion protein mol. to the subject, the **Ig** mol. having a variable region and a const. region, the **Ig** mol. being modified prior to administration by inactivation of at least a portion of the const. region. The **Ig** fusion protein is a **IgG**, **IgM**, or **IgA** which recognizes and binds **Ley** or **Le**. The **Ig** fusion protein may also be labeled with radiolabel, enzyme, chromophore, chemiluminescer or fluorescer for tumor diagnosis, or conjugates to cytotoxic agent for cancer therapy. **HBR96-2B**, **hBR96-2C**, **hBR96-2D**, **hBR96-2E**, **hBR96-2F**, **hBR96-2G**, and **hBR96-2H** are provided for the diagnosis and therapy purposes.

IT 203810-39-3 203810-42-8 203810-43-9  
203810-44-0 203810-45-1 203810-46-2  
203810-47-3 203810-48-4

RL: PRP (Properties)

(amino acid sequence; **Ig** fusion protein with mutated const. region for **inhibiting Ig.-induced toxicity** in **Ig** immunotherapy)

Searcher : Shears 308-4994

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1998 ACS  
 AN 1995:309167 CAPLUS  
 DN 122:95959  
 TI BR96-doxorubicin conjugate (BMS-182248) versus  
 doxorubicin: a comparative toxicity assessment in rats  
 AU Comereski, Charles R.; Peden, W. Michael; Davidson, Thomas J.;  
 Warner, Garvin L.; Hirth, Robert S.; Frantz, Jerry D.  
 CS Department of Biologics Evaluation, Bristol-Myers Squibb  
 Pharmaceutical Research Institute, Syracuse, NY, 13221-4755, USA  
 SO Toxicol. Pathol. (1994), 22(5), 473-88  
 CODEN: TOPADD; ISSN: 0192-6233  
 DT Journal  
 LA English  
 AB The toxicity of BMS-182248, an Ig (cBR96)-cytotoxic drug  
 (doxorubicin) conjugate, was investigated in Sprague-Dawley rats at  
 single i.v. doses of 508, 1,200, and 2,550 mg/m<sup>2</sup> (conjugated  
 doxorubicin doses of 14.7, 34.8, and 74 mg/m<sup>2</sup>, resp.) and compared  
 to that obtained from administration of free doxorubicin at single  
 doses of 33.6 and 72 mg/m<sup>2</sup> (approx. equiv. to that contained in the  
 1,200- and 2,550-mg/m<sup>2</sup> doses of BMS-182248, resp.). Necropsies were  
 conducted on day 8, upon death/moribund sacrifice, or after an  
 approx. 3-mo observation period following completion of treatment.  
 Death/moribundity of all rats that received 72 mg/m<sup>2</sup> and of 9 of 20  
 rats given 33.6 mg/m<sup>2</sup> free doxorubicin were attributed primarily to  
 delayed cardiotoxicity and glomerulonephropathy. With BMS-182248,  
 death from glomerulonephropathy and cardiotoxicity occurred in only  
 4 of 20 rats given 2,550 mg/m<sup>2</sup> (74 mg/m<sup>2</sup> doxorubicin equiv.). No  
 deaths or cardiotoxicity occurred in rats given 508 or 1,200 mg/m<sup>2</sup>  
 BMS-182248. Addnl. effects noted with either drug included  
 testicular atrophy, axonal degeneration of sciatic nerve and nerve  
 tracts of brain and spinal cord, teeth (incisor) abnormalities,  
 thymic atrophy, bone marrow hypocellularity, splenic lymphoid and  
 red-pulp depletion, and increased extra-medullary hematopoiesis in  
 the spleen and liver. Also noted were altered chief cells in the  
 stomach, vacuolation of adrenal gland and corpora lutea in the  
 ovary, uterine and seminal vesicle atrophy, ulceration and myocyte  
 regeneration/degeneration in the tongue, increased osteoclasts and  
 osteoblasts in bone, and lymphoid hyperplasia of mandibular lymph  
 node. In general, these effects were more severe in  
 doxorubicin-treated rats. All changes obsd. with BMS-182248 were  
 considered primarily due to the effects of doxorubicin and were  
 substantially less severe (most notably cardiotoxicity) compared to  
 those produced by an equiv. amt. of doxorubicin.

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1998 ACS  
 AN 1993:624155 CAPLUS  
 DN 119:224155  
 TI Phorbol ester, prostaglandin E2, forskolin and okadaic acid  
 differentially modulate interleukin-4-versus interleukin-2-dependent  
 Searcher : Shears 308-4994

immunoglobulin induction in human cellular models, in contrast to other selected modifiers of cellular activation

AU Armerding, Dieter; Hren, Andrea

CS Sandoz Forschungsinst., Vienna, Austria

SO Int. Arch. Allergy Immunol. (1993), 101(2), 143-52

CODEN: IAAIEG; ISSN: 1018-2438

DT Journal

LA English

AB Interleukin 2 (IL2) and 4 (IL4) are the most important mediators for Ig synthesis of human B lymphocytes. There is no obvious difference with regard to Ig isotypes induced by either lymphokine except for IgE; only IL4 induces this allergic antibody type.

**Monoclonal** anti-CD40 antibodies enhance both IL2- and IL4-dependent Ig induction. Searching for drugs which may inhibit induction of IgE but not of rather non-pathogenic Igs, the authors selected com. compds. which are commonly used as probes for transmembrane signalling pathways in other cellular systems. They included modulators of protein kinase C and intracellular calcium, inducers of cAMP, and inhibitors of protein tyrosine kinase, protein serine/threonine phosphatases and phosphodiesterases. The data presented suggest that IL2- and IL4-mediated B cell activation can be differentially modulated. Phorbol ester at non-cell-toxic doses inhibited IL4- but not IL2-dependent Ig induction. Prostaglandin E2 potentially enhanced IgE prodn. stimulated with IL4 alone but was inhibitory in the presence of anti-CD40 as a co-stimulatory signal. IgG1 responses elicited with IL2 plus anti-CD40, in contrast, were not affected. All other compds. did not discriminate between IL2- vs. IL4-mediated Ig induction.

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1998 ACS

AN 1991:119927 CAPLUS

DN 114:119927

TI Mechanism of Staphylococcus aureus exotoxin A inhibition of Ig production by human B cells

AU Moseley, Annemarie B.; Huston, David P.

CS Dep. Med., Baylor Coll. Med., Houston, TX, 77030, USA

SO J. Immunol. (1991), 146(3), 826-32

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The effects were examd. of Staphylococcus enterotoxin A (SEA) on proliferation and Ig prodn. of highly purified human B cells. The binding of SEA to MHC class II mols. on B cells does not alter their ability to proliferate in response to S. aureus Cowan strain I (SAC) or to produce Ig in response to SAC plus rIL-2. In contrast, the anti-DR mAb L243 inhibited both B cell proliferation and Ig prodn. Unable to det. a direct effect of SEA on B cell function, it was investigated whether the capacity of SEA to inhibit

Searcher : Shears 308-4994

SAC-induced Ig prodn. by PBMC was T cell-dependent. The results demonstrated that in the presence of T cells, under appropriate conditions, SEA can either function as a nominal antigen for stimulation of B cell proliferation and Ig prodn. or induce T cell-mediated suppression of Ig prodn. SEA-induced Ig prodn. required T cell help, which was dependent on pretreatment of the T cells with irradiation or mitomycin C; Ig prodn. was not induced by SEA in the absence of T cells or in the presence of untreated T cells. Furthermore, SEA inhibited Ig prodn. in SAC-stimulated cultures of autologous B cells and untreated T cells; pretreatment of the T cells with irradiation or mitomycin C abrogated SEA-induced inhibition of Ig prodn. Thus, T cell suppression of SAC-induced Ig prodn. was dependent on T cell proliferation. Similar results were observed with both SEA and toxic shock syndrome toxin 1.

=> d his 16- ful; d 1-32 .bevpat

FILE 'USPATFULL' ENTERED AT 16:24:45 ON 07 DEC 1998

L6 60 SEA ABB=ON PLU=ON L3(S)INHIBIT?

L7 32 SEA ABB=ON PLU=ON L6 AND (BR96 OR (BR OR CHIBR OR  
HBR) (W)96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR  
HB(W)(10460 OR 10036) OR MOAB OR MAB OR MONOCLON?)

L8 0 SEA ABB=ON PLU=ON L7 AND (LE OR LEY OR LEX)

L9 13 SEA ABB=ON PLU=ON L6 AND HYBRIDOMA

L10 32 SEA ABB=ON PLU=ON L7 OR L9

L10 ANSWER 1 OF 32 USPATFULL

AN 1998:150943 USPATFULL

TI Ras farnesyl transferase inhibitors

IN Marsters, Jr., James C., Oakland, CA, United States  
Brown, Michael S., Dallas, TX, United States  
Crowley, Craig W., Portola Valley, CA, United States  
Goldstein, Joseph L., Dallas, TX, United States  
James, Guy L., Dallas, TX, United States  
McDowell, Robert S., San Francisco, CA, United States  
Oare, David, Belmont, CA, United States  
Rawson, Thomas E., Mountain View, CA, United States  
Reynolds, Mark, South San Francisco, CA, United States  
Somers, Todd C., Foster City, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S.  
corporation)  
Board of Regents University of Texas, Austin, TX, United States  
(U.S. corporation)

PI US 5843941 981201  
WO 9426723 941124

AI US 94-313068 940926 (8)  
WO 94-US5157 940510  
940926 PCT 371 date  
940926 PCT 102(e) date  
Searcher : Shears 308-4994

RLI Continuation-in-part of Ser. No. US 93-82202, filed on 24 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-61961, filed on 14 May 1993, now abandoned

DT Utility

EXNAM Primary Examiner: Bond, Robert T.

LREP Winter, Daryl B.

CLMN Number of Claims: 17

ECL Exemplary Claim: 1,15

DRWN 21 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 8094

AB Benzodiazepine derivatives represented by the structure below are disclosed that act as potent inhibitors of ras farnesyl:protein transferase. Pharmaceutical compositions containing these benzodiazepines are provided for treatment of diseases for which inhibition of the ras farnesyl:protein transferase as indicated.  
##STR1##

INCL INCLM: 514/221.000  
INCLS: 540/509.000; 540/514.000

NCL NCLM: 514/221.000  
NCLS: 540/509.000; 540/514.000

L10 ANSWER 2 OF 32 USPATFULL

AN 1998:147244 USPATFULL

TI Recombinant lectins

IN Piatak, Jr., Michael, Walnut Creek, CA, United States

PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)

PI US 5840522 981124

AI US 95-437048 950509 (8)

RLI Continuation of Ser. No. US 86-837583, filed on 7 Mar 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-715934, filed on 25 Mar 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-653515, filed on 20 Sep 1984, now abandoned

DT Utility

EXNAM Primary Examiner: Degen, Nancy

LREP Marshall, O'Toole et al.; Blackburn, Robert P.

CLMN Number of Claims: 27

ECL Exemplary Claim: 1

DRWN 19 Drawing Figure(s); 19 Drawing Page(s)

LN.CNT 2412

AB DNA sequences encoding full length precursor proteins, which proteins contain both A and B portions of two ricin isotoxins and ricin agglutinin, as well as the linker regions have been determined. These DNAs or portions or modifications thereof are expressed in recombinant hosts to obtain the desired proteins or proteins which can readily converted thereto. One of the ricin isotoxins may be related to ricin E.

Searcher : Shears 308-4994

INCL INCLM: 435/069.100  
INCLS: 435/252.300; 435/252.330; 435/254.200; 435/254.210;  
435/320.100; 536/023.600  
NCL NCLM: 435/069.100  
NCLS: 435/252.300; 435/252.330; 435/254.200; 435/254.210;  
435/320.100; 536/023.600

## L10 ANSWER 3 OF 32 USPATFULL

AN 1998:79186 USPATFULL  
TI Use of quinoline-3-carboxamide compounds for inhibiting the  
production of tumor necrosis factor (TNF) and/or for the treatment  
of septic shock  
IN Kroemer, Guido Peter, Madrid, Spain  
Gonzalo, JoseAngel, Madrid, Spain  
Alonso, Carlos Martinez, Madrid, Spain  
Kalland, Terje, Loddekoping, Sweden  
PA Pharmacia AB, Stockholm, Sweden (non-U.S. corporation)  
PI US 5776947 980707  
WO 9503051 950202  
AI US 96-586857 960520 (8)  
WO 94-SE565 940610  
960520 PCT 371 date  
960520 PCT 102(e) date  
PRAI SE 93-2490 930726  
DT Utility  
EXNAM Primary Examiner: Goldberg, Jerome D.  
LREP Lowe, Price, LeBlanc & Becker  
CLMN Number of Claims: 5  
ECL Exemplary Claim: 1  
DRWN 4 Drawing Figure(s); 3 Drawing Page(s)  
LN.CNT 535

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of a quinoline-3-carboxamide compound comprising structure  
(I), optionally with substituents for the hydrogen atoms shown  
(H.sup.1-9), and a salt of compound (I) where (a) ---- represents  
that there are two conjugated double bonds between the atoms  
comprised by the dashed line, (b) X.sub.1 and X.sub.2 are  
separately selected from an oxygen atom or an NH.sup.9 group, said  
X.sub.1 and X.sub.2 being bound by a single bond to the ring when  
attached to H.sup.7 or H.sup.8 and by a double bond when not bound  
to H.sup.7 or H.sup.8, (c) H.sup.1-9 ; are hydrogens with the  
provision that H.sup.9 is only present when at least one of  
X.sub.1 and X.sub.2 is the NH.sup.9 group, (d) H.sup.7 and H.sup.8  
are hydrogens that are attached to different atoms selected among  
X.sub.1, X.sub.2 and the nitrogen atom (N) in the quinoline ring,  
for the manufacture of a composition intended for inhibiting the  
production of tumor necrosis factor TNF in a living body and/or  
the treatment of septic shock in a living body.

Searcher : Shears 308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/312.000  
INCLS: 514/313.000  
NCL NCLM: 514/312.000  
NCLS: 514/313.000

L10 ANSWER 4 OF 32 USPATFULL

AN 1998:28189 USPATFULL  
TI Anti-idiotypic antibody composition for inhibiting acute  
complement-mediated cytotoxicity  
IN Koren, Eugen, Oklahoma City, OK, United States  
Cooper, David K. C., Oklahoma City, OK, United States  
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United  
States (U.S. corporation)  
Baptist Medical Center of Oklahoma, Inc., Oklahoma City, OK,  
United States (U.S. corporation)  
PI US 5728812 980317  
AI US 95-458274 950602 (8)  
RLI Division of Ser. No. US 93-133934, filed on 12 Oct 1993, now  
patented, Pat. No. US 5560911  
DT Utility  
EXNAM Primary Examiner: Loring, Susan A.  
LREP Arnall Golden & Gregory, LLP  
CLMN Number of Claims: 14  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1171

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Antibodies directed against idiotypes on naturally occurring human  
anti-animal antibodies are disclosed for use in inhibiting  
xenograft rejection in human patients. An effective quantity of  
these anti-idiotypic antibodies is injected into the actual or  
potential xenograft recipient in order to bind to the idiotypes  
expressed on anti-animal antibodies as well as subpopulations of B  
lymphocytes, to inhibit hyperacute rejection of transplanted  
animal tissues or organs by the human patient. Alternatively,  
anti-idiotypic antibodies are used in the form of immunoaffinity  
columns to deplete anti-animal antibodies from the recipient's  
serum. Methods of making mouse monoclonal, mouse  
recombinant, and human recombinant anti-idiotypic antibodies are  
described, as well as immunoaffinity columns containing  
immobilized anti-idiotypic antibodies. A method and means for  
assessing the expected character and severity of a patient's  
rejection response to transplanted animal tissues is described, as  
well as methods of identification, isolation and suppression of  
lymphocytes bearing anti-animal idiotypes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Searcher : Shears 308-4994



08/905293

INCL INCLM: 530/387.200  
INCLS: 530/387.100; 530/387.500; 530/391.300; 530/391.100  
NCL NCLM: 530/387.200  
NCLS: 530/387.100; 530/387.500; 530/391.100; 530/391.300

L10 ANSWER 5 OF 32 USPATFULL

AN 1998:14798 USPATFULL  
TI Tricyclic inhibitors of the vitronectin receptor  
IN Blackburn, Brent K., San Francisco, CA, United States  
Robarge, Kirk, San Francisco, CA, United States  
Somers, Todd C., Foster City, CA, United States  
PA Genentech, Inc., South San Francisco, CA, United States (U.S.  
corporation)  
PI US 5716951 980210  
AI US 95-438143 950508 (8)  
RLI Division of Ser. No. US 94-313069, filed on 29 Sep 1994, now  
patented, Pat. No. US 5602173 And a continuation-in-part of Ser.  
No. US 93-99019, filed on 29 Jul 1993, now patented, Pat. No. US  
5493020  
DT Utility  
EXNAM Primary Examiner: Bond, Robert T.  
LREP Winter, Daryl B.  
CLMN Number of Claims: 7  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 3731

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A tricyclic benzodiazepine derivative that acts as a nonpeptidyl  
platelet aggregation inhibitor is provided. This inhibitor  
potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a  
receptor and is provided in therapeutic compositions for the  
treatment of diseases for which blocking platelet aggregation is  
indicated. These nonpeptidyl inhibitors are provided in  
combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/219.000  
INCLS: 514/220.000; 540/497.000; 540/498.000  
NCL NCLM: 514/219.000  
NCLS: 514/220.000; 540/497.000; 540/498.000

L10 ANSWER 6 OF 32 USPATFULL

AN 1998:11701 USPATFULL  
TI IL-4 bone therapy  
IN Lewis, David B., Seattle, WA, United States  
Perlmutter, Roger M., Seattle, WA, United States  
PA Board of Regents of the University of Washington, Seattle, WA,  
United States (U.S. corporation)  
PI US 5714146 980203

Searcher : Shears 308-4994

08/905293

AI US 95-418826 950407 (8)  
RLI Continuation of Ser. No. US 92-935891, filed on 26 Aug 1992, now abandoned  
DT Utility  
EXNAM Primary Examiner: Ziska, Suzanne E.  
LREP Christensen O'Connor Johnson & Kindness PLLC  
CLMN Number of Claims: 1  
ECL Exemplary Claim: 1  
DRWN 11 Drawing Figure(s); 7 Drawing Page(s)  
LN.CNT 2044

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An in vivo assay for selecting a candidate therapeutic for treating osteoporosis. A candidate reagent is administered to an IL-4 transgenic mammal whose cells contain a recombinant IL-4 coding sequence operably lined to a promoter sequence which is transcriptionally active in bone marrow cells. At the time the candidate reagent is first administered the IL-4 transgenic mammal is either symptomatic of, or asymptomatic of, an osteoporotic phenotype. The candidate reagent is selected as a candidate therapeutic for treating osteoporosis if either amelioration of, or delay in the onset of, the osteoporotic phenotype is observed following administration of the candidate reagent to the IL-4 transgenic mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/130.100  
INCLS: 800/002.000; 424/143.100; 424/145.100; 424/152.100;  
424/184.100  
NCL NCLM: 424/130.100  
NCLS: 424/143.100; 424/145.100; 424/152.100; 424/184.100

L10 ANSWER 7 OF 32 USPATFULL

AN 1998:7173 USPATFULL

TI Method of causing selective immunosuppression using HL-60-related lectins

IN Seilhamer, Jeffrey J., 118a Moulton Dr., Milpitas, CA, United States 95035  
Nedwin, Glenn, 3245 Oyster Bay Ave., Davis, CA, United States 95616  
Bringman, Tim, 817 Santa Florencia, Solana Beach, CA, United States 92075  
Couraud, Pierre-Olivier, Auffargis, 9 rue du Perray, 78610 Le Perray, France

PI US 5710257 980120

AI US 96-719551 960925 (8)

RLI Division of Ser. No. US 94-326739, filed on 20 Oct 1994 which is a continuation of Ser. No. US 92-976928, filed on 16 Nov 1992, now abandoned which is a continuation-in-part of Ser. No. US 89-313649, filed on 21 Feb 1989, now abandoned which is a

Searcher : Shears 308-4994

08/905293

continuation-in-part of Ser. No. US 88-263734, filed on 28 Oct 1988, now abandoned which is a continuation-in-part of Ser. No. US 88-181747, filed on 14 Apr 1988, now abandoned

DT Utility  
EXNAM Primary Examiner: Ziska, Suzanne E.  
LREP Morrison & Foerster  
CLMN Number of Claims: 8  
ECL Exemplary Claim: 1  
DRWN 15 Drawing Figure(s); 13 Drawing Page(s)  
LN.CNT 1513

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical compositions useful in the treatment of autoimmune conditions include as an active ingredient a soluble lectin having a molecular weight of about 14 kilodaltons or a fragment thereof. The lectin or fragment binds .beta.-galactoside-containing moieties independent of the presence or absence of Ca.sup.+2, stimulates hemagglutination of trypsinized rabbit erythrocytes in standard lectin assays wherein the stimulation is inhibited by lactose or thiogalactoside, has an amino acid sequence containing at least one N-glycosylation site and is at least 90% homologous to the amino acid sequence shown in positions 2-135 of FIG. 1 or the relevant portions thereof. The composition is used for treatment of autoimmune conditions such as rheumatoid arthritis, myasthenia gravis, and multiple sclerosis, as well as modulating the immune response in an allergic reactions or to organ or tissue transplant rejection. The inventive composition can be combined with general immunosuppressants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/396.000  
INCLS: 530/350.000; 435/172.300  
NCL NCLM: 530/396.000  
NCLS: 530/350.000

L10 ANSWER 8 OF 32 USPATFULL

AN 1998:4562 USPATFULL  
TI Methods of using growth inhibitory peptides  
IN Mizejewski, Gerald J., Clifton Park, NY, United States  
PA Health Research, Incorporated, Albany, NY, United States (U.S. corporation)  
PI US 5707963 980113  
AI US 96-636386 960423 (8)  
RLI Continuation-in-part of Ser. No. US 94-329506, filed on 26 Oct 1994  
DT Utility  
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Pak, Michael D.  
LREP Jaeckle Fleischmann & Mugel, LLP  
CLMN Number of Claims: 12

Searcher : Shears 308-4994

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1202

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The subject invention provides non-naturally occurring peptides capable of inhibiting growth factor-stimulated growth of cells. The peptide can be utilized to inhibit growth factor-stimulated growth, such growth factors including, for example, gonadotropins, peptide hormones, synthetic growth factors, and ligands, the ligand having a receptor that is a member of the steroid/thyroid hormone/vitamin receptor superfamily. Also provided are DNA sequences encoding the peptides and methods of producing and using the peptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/012.000

INCLS: 435/375.000; 530/324.000

NCL NCLM: 514/012.000

NCLS: 435/375.000; 530/324.000

L10 ANSWER 9 OF 32 USPATFULL

AN 1998:2162 USPATFULL

TI Tricyclic inhibitors of the GPII.sub.b III.sub.a receptor

IN Blackburn, Brent K., San Francisco, CA, United States

Robarge, Kirk, San Francisco, CA, United States

Somers, Todd C., Foster City, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 5705890 980106

WO 9504057 950209

AI US 94-313069 940926 (8)

WO 94-US7989 940715

940926 PCT 371 date

940926 PCT 102(e) date

RLI Continuation-in-part of Ser. No. US 93-99019, filed on 29 Jul 1993, now patented, Pat. No. US 5493020, issued on 20 Feb 1996

DT Utility

EXNAM Primary Examiner: Bond, Robert T.

LREP Winter, Daryl B.

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4804

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A tricyclic benzodiazepine derivative that acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is

Searcher : Shears 308-4994

indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 314/220.000  
INCLS: 514/219.000; 540/497.000; 540/498.000  
NCL NCLM: 514/220.000  
NCLS: 514/219.000; 540/487.000; 540/498.000

L10 ANSWER 10 OF 32 USPATFULL

AN 97:112586 USPATFULL

TI Method of causing selective immunosuppression using HL-60 related lectins

IN Seilhammer, Jeffrey J., Milpitas, CA, United States

Nedwin, Glenn, Davis, CA, United States

Bringman, Tim, Solana Beach, CA, United States

Couraud, Pierre-Olivier, Auffargis, France

PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

PI US 5693760 971202

AI US 94-326739 941020 (8)

RLI Continuation of Ser. No. US 92-976928, filed on 16 Nov 1992, now abandoned which is a continuation-in-part of Ser. No. US 89-313649, filed on 21 Feb 1989, now abandoned which is a continuation-in-part of Ser. No. US 88-263734, filed on 28 Oct 1988, now abandoned which is a continuation-in-part of Ser. No. US 88-181747, filed on 14 Apr 1988, now abandoned

DT Utility

EXNAM Primary Examiner: Ziska, Suzanne E.

LREP Morrison & Foerster

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN 15 Drawing Figure(s); 13 Drawing Page(s)

LN.CNT 1533

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical compositions useful in the treatment of autoimmune conditions include as an active ingredient a soluble lectin having a molecular weight of about 14 kilodaltons or a fragment thereof. The lectin or fragment binds .beta.-galactoside-containing moieties independent of the presence or absence of Ca.sup.+2, stimulates hemagglutination of trypsinized rabbit erythrocytes in standard lectin assays wherein the stimulation is inhibited by lactose or thiogalactoside, has an amino acid sequence containing at least one N-glycosylation site and is at least 90% homologous to the amino acid sequence shown in positions 2-135 of FIG. 1 or the relevant portions thereof. The composition is used for treatment of autoimmune conditions such as rheumatoid arthritis, myasthenia gravis, and multiple sclerosis, as well as modulating the immune response in an allergic reactions or to organ or tissue

Searcher : Shears 308-4994

08/905293

transplant rejection. The inventive composition can be combined with general immunosuppressants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/396.000  
INCLS: 530/350.000; 530/827.000; 435/172.300; 424/278.100  
NCL NCLM: 530/396.000  
NCLS: 424/278.100; 514/008.000; 530/350.000; 530/827.000

L10 ANSWER 11 OF 32 USPATFULL

AN 97:104105 USPATFULL

TI Epitope-specific **monoclonal** antibodies and immunotoxins and uses thereof

IN Uhr, Jonathan W., Dallas, TX, United States

Vitetta, Ellen S., Dallas, TX, United States

Scheuermann, Richard H., Carrollton, TX, United States

PA Board of Regents, The University of Texas, Austin, TX, United States (U.S. corporation)

PI US 5686072 971111

AI US 94-202042 940222 (8)

RLI Continuation-in-part of Ser. No. US 92-899781, filed on 17 Jun 1992, now abandoned

DT Utility

EXNAM Primary Examiner: Scheiner, Toni R.

LREP Arnold White & Durkee

CLMN Number of Claims: 32

ECL Exemplary Claim: 1

DRWN 12 Drawing Figure(s); 11 Drawing Page(s)

LN.CNT 2395

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The anti-tumor activity of a mixture of anti-CD22 and anti-CD19 immunotoxins is shown to be significantly enhanced in SCID/Daudi mice with disseminated human Daudi lymphoma. Unexpectedly identical enhancement was observed employing a combination of the anti-CD22 immunotoxin with unconjugated anti-CD19 antibodies. Thus combinations of an anti-CD22 immunotoxin and an anti-CD19 immunotoxin or antibody act synergistically and provide advantageous compositions and methods for immunotherapeutic treatment of various diseases including cancer and autoimmune disorders. Also disclosed is data indicating that certain anti-CD19 antibodies alone inhibit proliferation of CD19-positive cells by inducing cell cycle arrest.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/183.100  
INCLS: 530/391.700; 530/388.730; 435/007.240  
NCL NCLM: 424/183.100  
NCLS: 435/007.240; 530/388.730; 530/391.700

Searcher : Shears 308-4994

L10 ANSWER 12 OF 32 USPATFULL

AN 97:91522 USPATFULL

TI Nonpeptidyl integrin inhibitors having specificity for the  
GPII.sub.b III.sub.a

IN Blackburn, Brent, San Francisco, CA, United States

Barker, Peter, El Granada, CA, United States

Gadek, Thomas, Oakland, CA, United States

McDowell, Robert, San Francisco, CA, United States

McGee, Lawrence, Pacifica, CA, United States

Somers, Todd, Montara, CA, United States

Webb, Rob, Moss Beach, CA, United States

Robarge, Kirk, San Francisco, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S.  
corporation)

PI US 5674865 971007

AI US 95-451794 950526 (8)

RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993, now  
abandoned which is a continuation-in-part of Ser. No. US  
92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679  
which is a continuation-in-part of Ser. No. US 91-781477, filed on  
18 Oct 1991, now abandoned

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Wong, King  
Lit

LREP Winter, Daryl B.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 13454

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzodiazepinedione derivative which acts as a nonpeptidyl  
platelet aggregation inhibitor is provided. This inhibitor  
potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a  
receptor and is provided in therapeutic compositions for the  
treatment of diseases for which blocking platelet aggregation is  
indicated. These nonpeptidyl inhibitors are provided in  
combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/213.000

INCLS: 514/215.000; 514/219.000; 514/220.000; 514/221.000;  
540/523.000; 540/580.000; 540/593.000; 540/495.000;  
540/506.000; 540/490.000; 540/493.000; 540/504.000;  
540/512.000

NCL NCLM: 514/213.000

NCLS: 514/215.000; 514/219.000; 514/220.000; 514/221.000;  
540/490.000; 540/493.000; 540/495.000; 540/504.000;  
540/506.000; 540/512.000; 540/523.000; 540/580.000;  
540/593.000

Searcher : Shears 308-4994

L10 ANSWER 13 OF 32 USPATFULL

AN 97:91520 USPATFULL

TI Nonpeptidyl integrin inhibitors having specificity for the GPII.sub.b III.sub.a receptor

IN Blackburn, Brent, San Francisco, CA, United States

Barker, Peter, El Granada, CA, United States

Gadek, Thomas, Oakland, CA, United States

McDowell, Robert, San Francisco, CA, United States

McGee, Lawrence, Pacifica, CA, United States

Somers, Todd, Montara, CA, United States

Webb, Rob, Moss Beach, CA, United States

Robarge, Kirk, San Francisco, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 5674863 971007

AI US 95-451849 950526 (8)

RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Wong, King Lit

LREP Winter, Daryl B.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 13521

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/211.000

INCLS: 540/490.000; 540/552.000; 540/523.000; 540/580.000;  
540/593.000; 540/495.000; 540/506.000; 540/493.000;  
540/504.000; 540/512.000; 514/215.000; 514/219.000;  
514/220.000; 514/221.000

NCL NCLM: 514/211.000

NCLS: 514/215.000; 514/219.000; 514/220.000; 514/221.000;  
540/490.000; 540/493.000; 540/495.000; 540/504.000;  
540/506.000; 540/512.000; 540/523.000; 540/552.000;

Searcher : Shears 308-4994



08/905293

540/580.000; 540/593.000

L10 ANSWER 14 OF 32 USPATFULL

AN 97:78435 USPATFULL

TI Nonpeptidyl integrin inhibitors having specificity for the  
GPII.sub.b III.sub.a receptor

IN Blackburn, Brent, San Francisco, CA, United States

Barker, Peter, El Granada, CA, United States

Gadek, Thomas, Oakland, CA, United States

McDowell, Robert, San Francisco, CA, United States

McGee, Lawrence, Pacifica, CA, United States

Somers, Todd, Montara, CA, United States

Webb, Rob, Moss Beach, CA, United States

Robarge, Kirk, San Francisco, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S.  
corporation)

PI US 5663166 970902

AI US 95-452056 950526 (8)

RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993, now  
abandoned which is a continuation-in-part of Ser. No. US  
92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679  
which is a continuation-in-part of Ser. No. US 91-781477, filed on  
18 Oct 1991, now abandoned

DT Utility

EXNAM Primary Examiner: Bond, Robert T.

LREP Winter, Daryl B.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 13432

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzodiazepinedione derivative which acts as a nonpeptidyl  
platelet aggregation inhibitor is provided. This inhibitor  
potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a  
receptor and is provided in therapeutic compositions for the  
treatment of diseases for which blocking platelet aggregation is  
indicated. These nonpeptidyl inhibitors are provided in  
combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/213.000

INCLS: 514/215.000; 514/217.000; 540/522.000; 540/523.000;  
540/521.000

NCL NCLM: 514/213.000

NCLS: 514/215.000; 514/217.000; 540/521.000; 540/522.000;  
540/523.000

L10 ANSWER 15 OF 32 USPATFULL

AN 97:27048 USPATFULL

Searcher : Shears 308-4994

TI Tripterygium wilfordii hook F extracts and components, and uses thereof

IN Lipsky, Peter E., Dallas, TX, United States  
 Tao, Xue-Lian, Dallas, TX, United States  
 Cai, Jian, Dallas, TX, United States  
 Kovacs, William J., Nashville, TN, United States  
 Olsen, Nancy J., Nashville, TN, United States

PA Board of Regents, University of TX System, Austin, TX, United States (U.S. corporation)

PI US 5616458 970401

AI US 95-455906 950531 (8)

RLI Continuation-in-part of Ser. No. US 93-168980, filed on 17 Dec 1993 which is a continuation-in-part of Ser. No. US 92-862836, filed on 3 Apr 1992, now patented, Pat. No. US 5294443, issued on 15 Mar 1994 which is a continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned

DT Utility

EXNAM Primary Examiner: Rollins, John W.

LREP Mayfield, Denise L.

CLMN Number of Claims: 6

ECL Exemplary Claim: 1

DRWN 59 Drawing Figure(s); 25 Drawing Page(s)

LN.CNT 3010

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides for the use of Tripterygium wilfordii Hook F extracts and purified components thereof in the treatment of inflammation or an immune disorder with concomitant lack of steroidal effect. Extracts of this plant (T2) bound to the glucocorticoid receptor and competitively inhibited glucocorticoid mediated cellular processes, such as dexamethasone binding to the glucocorticoid receptor, glucocorticoid mediated activation of target genes, dexamethasone dependent cellular growth, with concomitant inhibition of cyclooxygenase-2 induction and inflammatory processes such as the production of prostaglandin E.sub.2. The T2 extract components triptolide and triptolide were effective inhibitors. The particular advantage provided by the methods herein is the treatment or prevention of inflammation and the concomitant lack of steroidal agonist effects and NSAID side effects. Conditions treatable by the present methods include inflammation and immune disorders including autoimmune disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/004.000  
 INCLS: 435/007.500; 435/007.900; 424/078.050; 424/195.100;  
 514/469.000; 514/821.000; 514/825.000; 514/886.000

NCL NCLM: 435/004.000  
 NCLS: 424/078.050; 424/195.100; 435/007.500; 435/007.900;  
 514/469.000; 514/821.000; 514/825.000; 514/886.000

L10 ANSWER 16 OF 32 USPATFULL

AN 97:1356 USPATFULL

TI Anthrax toxin fusion proteins, nucleic acid encoding same

IN Leppla, Stephen H., Bethesda, MD, United States

Klimpel, Kurt R., Gaithersburg, MD, United States

Arora, Naveen, Delhi, India

Singh, Yogendra, Delhi, India

Nicholls, Peter J., Welling Kent, United Kingdom

PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

PI US 5591631 970107

AI US 93-21601 930212 (8)

DT Utility

EXNAM Primary Examiner: Walsh, Stephen G.

LREP Townsend and Townsend and Crew

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2181

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a nucleic acid encoding a fusion protein, comprising a nucleotide sequence encoding the protective antigen (PA) binding domain of the native lethal factor (LF) protein and a nucleotide sequence encoding an activity inducing domain of a second protein. Also provided is a nucleic acid encoding a fusion protein, comprising a nucleotide sequence encoding the translocation domain and LF binding domain of the native PA protein and a nucleotide sequence encoding a ligand domain which specifically binds a cellular target. Proteins encoded by the nucleic acid of the invention, vectors comprising the nucleic acids and hosts capable of expressing the protein encoded by the nucleic acids are also provided. A composition comprising the PA binding domain of the native LF protein chemically attached to a non-LF activity inducing moiety is further provided. A method for delivering an activity to a cell is provided. The steps of the method include administering to the cell a protein comprising the translocation domain and the LF binding domain of the native PA protein and a ligand domain, and administering to the cell a product comprising the PA binding domain of the native LF protein and a non-LF activity inducing moiety, whereby the product administered is internalized into the cell and performs the activity within the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/252.300

INCLS: 435/320.100; 536/023.400; 536/023.700; 530/350.000;  
530/402.000

NCL NCLM: 435/252.300

Searcher : Shears 308-4994

08/905293

NCLS: 435/320.100; 530/350.000; 530/402.000; 536/023.400;  
536/023.700

L10 ANSWER 17 OF 32 USPATFULL

AN 96:111153 USPATFULL

TI Preparations and uses thereof for immunosuppression

IN Lipsky, Peter E., Dallas, TX, United States

Tao, Xue L., Dallas, TX, United States

Cai, Jian, Dallas, TX, United States

PA Board of Regents The University of Texas System, Austin, TX,  
United States (U.S. corporation)

PI US 5580562 961203

AI US 93-168980 931217 (8)

RLI Continuation-in-part of Ser. No. US 92-862836, filed on 3 Apr  
1992, now patented, Pat. No. US 5294443 which is a  
continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar  
1990, now abandoned

DT Utility

EXNAM Primary Examiner: Robinson, Douglas W.; Assistant Examiner: Lee,  
Howard C.

LREP Akin, Gump, Strauss, Hauer & Feld, L.L.P.

CLMN Number of Claims: 17

ECL Exemplary Claim: 1

DRWN 43 Drawing Figure(s); 19 Drawing Page(s)

LN.CNT 2140

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A Tripterygium wilfordii Hook F preparation having an improved  
LD.sub.50 in mice, an improved therapeutic activity:toxic index  
ratio and a lower amount of triptolide as compared to previous  
preparations is disclosed. The LD.sub.50 in mice of the T.  
wilfordii preparation is greater than about 860 mg/kg, the  
therapeutic activity:toxic index ratio is greater than about  
2.6.times.10.sup.-3, and the amount of triptolide is less than  
about 1.3 .mu.g/mg. The preparation is useful for  
immunosuppression, in particular, the suppression of primary  
antibody response and suppression of autoimmune disease and for  
the treatment of rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/195.100

INCLS: 514/885.000; 514/908.000; 549/228.000; 549/297.000;  
549/298.000

NCL NCLM: 424/195.100

NCLS: 514/885.000; 514/908.000; 549/228.000; 549/297.000;  
549/298.000

L10 ANSWER 18 OF 32 USPATFULL

AN 96:94579 USPATFULL

TI Nonpeptidyl integrin inhibitors having specificity for the  
Searcher : Shears 308-4994

GPII.sub.b III.sub.a receptor

IN Blackburn, Brent, San Francisco, CA, United States  
 Barker, Peter, El Granada, CA, United States  
 Gadek, Thomas, Oakland, CA, United States  
 McDowell, Robert, San Francisco, CA, United States  
 McGee, Lawrence, Pacifica, CA, United States  
 Somers, Todd, Montara, CA, United States  
 Webb, Rob, Moss Beach, CA, United States  
 Robarge, Kirk, San Francisco, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 5565449 961015

AI US 95-452479 950526 (8)

RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993 which is a continuation-in-part of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned

DT Utility

EXNAM Primary Examiner: Bond, Robert T.

LREP Winter, Daryl B.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1,2

DRWN No Drawings

LN.CNT 13455

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/219.000  
 INCLS: 514/220.000; 514/221.000; 540/493.000; 540/495.000;  
 540/504.000; 540/512.000

NCL NCLM: 514/219.000  
 NCLS: 514/220.000; 514/221.000; 540/493.000; 540/495.000;  
 540/504.000; 540/512.000

L10 ANSWER 19 OF 32 USPATFULL

AN 96:89627 USPATFULL

TI Method of inhibiting acute complement mediated cytotoxicity with anti-idiotypic antibodies

IN Koren, Eugen, Oklahoma City, OK, United States  
 Cooper, David K. C., Oklahoma City, OK, United States

PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United States  
 Searcher : Shears 308-4994

08/905293

States (U.S. corporation)  
Integris Baptist Medical Center, Inc., Oklahoma City, OK, United  
States (U.S. corporation)  
PI US 5560911 961001  
AI US 93-133934 931012 (8)  
DT Utility  
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Loring, Susan  
A.  
LREP Arnall Golden & Gregory  
CLMN Number of Claims: 10  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1164

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Antibodies directed against idiotypes on naturally occurring human anti-animal antibodies are disclosed for use in inhibiting xenograft rejection in human patients. An effective quantity of these anti-idiotypic antibodies is injected into the actual or potential xenograft recipient in order to bind to the idiotypes expressed on anti-animal antibodies as well as subpopulations of B lymphocytes, to inhibit hyperacute rejection of transplanted animal tissues or organs by the human patient. Alternatively, anti-idiotypic antibodies are used in the form of immunoaffinity columns to deplete anti-animal antibodies from the recipient's serum. Methods of making mouse monoclonal, mouse recombinant, and human recombinant anti-idiotypic antibodies are described, as well as immunoaffinity columns containing immobilized anti-idiotypic antibodies. A method and means for assessing the expected character and severity of a patient's rejection response to transplanted animal tissues is described, as well as methods of identification, isolation and suppression of lymphocytes bearing anti-animal idiotypes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/131.100  
INCLS: 424/140.100; 530/387.200  
NCL NCLM: 424/131.100  
NCLS: 424/140.100; 530/387.200

L10 ANSWER 20 OF 32 USPATFULL

AN 96:23023 USPATFULL  
TI Inhibition of IL-2 production by Tripterygium wilfordii Hook F extract  
IN Lipsky, Peter E., Dallas, TX, United States  
Tao, Xue-Lian, Dallas, TX, United States  
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)  
PI US 5500340 960319  
AI US 93-136345 931014 (8)

Searcher : Shears 308-4994

RLI Division of Ser. No. US 92-862836, filed on 3 Apr 1992, now patented, Pat. No. US 5294443, issued on 15 Mar 1994 which is a continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned

DT Utility

EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Myers, Carla

LREP Akin, Gump, Strauss, Hauer & Feld

CLMN Number of Claims: 3

ECL Exemplary Claim: 1

DRWN 35 Drawing Figure(s); 14 Drawing Page(s)

LN.CNT 1248

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention involves the use of Tripterygium Wilfordii Hook F extracts in the treatment of rheumatoid arthritis. An alcohol extract of this plant (T2) inhibited antigen- and mitogen-stimulated proliferation of T cells and B cells, cell cycle progression, interleukin-2 (IL-2) production by T cells, immunoglobulin production by B cells and interleukin-2 mRNA production. T2 did not affect IL-2 receptor expression by T cells, IL-1 production by monocytes, the capacity of monocytes to present antigen, or signaling pathways. Inhibition could not be accounted for by nonspecific toxicity. These results support the conclusion that T2 exerts a powerful suppressive effect on human immune responses. Suppressing autoimmune disease is a most preferred embodiment of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/006.000  
INCLS: 436/063.000; 935/034.000; 935/077.000

NCL NCLM: 435/006.000  
NCLS: 436/063.000

L10 ANSWER 21 OF 32 USPATFULL

AN 96:14918 USPATFULL

TI Tricyclic inhibitors of the GPII.sub.b III.sub.a receptor

IN Blackburn, Brent K., San Francisco, CA, United States  
Robarge, Kirk, San Francisco, CA, United States  
Somers, Todd C., Montara, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 5493020 960220

AI US 93-99019 930729 (8)

DT Utility

EXNAM Primary Examiner: Bond, Robert T.

LREP Winter, Daryl B.

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

DRWN No Drawings

Searcher : Shears 308-4994

LN.CNT 3570

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A trycyclic benzodiazepine derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 540/498.000

NCL NCLM: 540/498.000

L10 ANSWER 22 OF 32 USPATFULL

AN 95:29638 USPATFULL

TI Benzazepine platelet aggregation inhibitors having specificity for the GPII.sub.b III.sub.a receptor

IN Blackburn, Brent, San Francisco, CA, United States

McDowell, Robert, San Francisco, CA, United States

Gadek, Thomas, Oakland, CA, United States

Webb, Rob, Moss Beach, CA, United States

PA Genentech, Inc., So. San Francisco, CA, United States (U.S. corporation)

PI US 5403836 950404

AI US 93-58722 930506 (8)

RLI Division of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Datlow, Philip I.

LREP Winter, Daryl B.

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 11322

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzazepine derivative that acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/213.000

INCLS: 540/495.000; 540/506.000; 540/523.000

Searcher : Shears 308-4994



NCL NCLM: 514/213.000  
NCLS: 540/495.000; 540/506.000; 540/523.000

L10 ANSWER 23 OF 32 USPATFULL

AN 94:22078 USPATFULL  
TI Tripterygium wilford II hook f extracts and components thereof for immunosuppression  
IN Lipsky, Peter E., Dallas, TX, United States  
Tao, Xue-Lian, Dallas, TX, United States  
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)  
PI US 5294443 940315  
AI US 92-862836 920403 (7)  
RLI Continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned  
DT Utility  
EXNAM Primary Examiner: Rollins, John W.  
LREP Arnold, White & Durkee  
CLMN Number of Claims: 10  
ECL Exemplary Claim: 1  
DRWN 35 Drawing Figure(s); 14 Drawing Page(s)  
LN.CNT 1210

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention involves the use of Tripterygium Wilfordii Hook F extracts in the treatment of rheumatoid arthritis. An alcohol extract of this plant (T2) **inhibited** antigen- and mitogen-stimulated proliferation of T cells and B cells, cell cycle progression, interleukin-2 (IL-2) production by T cells, **immunoglobulin** production by B cells and interleukin-2 mRNA production. T2 did not affect IL-2 receptor expression by T cells, IL-1 production by monocytes, the capacity of monocytes to present antigen, or signaling pathways. **Inhibition** could not be accounted for by nonspecific **toxicity**. These results support the conclusion that T2 exerts a powerful suppressive effect on human immune responses. Suppressing autoinnate disease is a most preferred embodiment of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/195.100  
INCLS: 514/885.000  
NCL NCLM: 424/195.100  
NCLS: 514/885.000

L10 ANSWER 24 OF 32 USPATFULL

AN 94:9659 USPATFULL  
TI Method of producing immune response  
IN Berzofsky, Jay A., Bethesda, MD, United States  
Kawamura, Hajime, Tochigi, Japan  
Searcher : Shears 308-4994

PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

PI US 5283323 940201

AI US 91-715712 910618 (7)

RLI Continuation of Ser. No. US 89-338362, filed on 13 Apr 1989, now abandoned which is a continuation of Ser. No. US 85-763218, filed on 7 Aug 1985, now abandoned

DT Utility

EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Carlson, K. Cochrane

LREP Birch, Stewart, Kolasch & Birch

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 10 Drawing Page(s)

LN.CNT 743

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention discloses a process for enhancing antibody response to an antigen. A novel step in the process is the preparation of a conjugate of the antigen with an anti-immunoglobulin. The conjugate thus prepared is then administered to a host for in vivo effect or presented to T and B cells in a suitable culture system for in vitro response. The present invention by increasing immunogenicity makes it possible to produce antibodies against very low doses of antigens and otherwise weak or insufficient antigens or synthetic vaccines.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/387.100  
INCLS: 530/387.300; 530/391.700; 424/085.910

NCL NCLM: 424/178.100  
NCLS: 424/153.100; 424/173.100; 424/193.100; 530/387.300;  
530/388.730; 530/389.600; 530/391.700

L10 ANSWER 25 OF 32 USPATFULL

AN 93:82994 USPATFULL

TI Nonpeptidyl platelet aggregation inhibitors having specificity for the GPII.sub.b III.sub. receptor

IN Blackburn, Brent, San Francisco, CA, United States  
McDowell, Robert, San Francisco, CA, United States  
Gadek, Thomas, Oakland, CA, United States  
Barker, Peter, El Granada, CA, United States  
McGee, Lawrence, Pacifica, CA, United States  
Webb, Rob, Moss Beach, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 5250679 931005

AI US 92-866931 920410 (7)

RLI Continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct  
Searcher : Shears 308-4994

08/905293

1991, now abandoned  
DT Utility  
EXNAM Primary Examiner: Bond, Robert T.  
LREP Winter, Daryl B.  
CLMN Number of Claims: 1  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 10784

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potentially inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 540/490.000  
INCLS: 540/495.000; 540/512.000; 540/523.000  
NCL NCLM: 540/490.000  
NCLS: 540/495.000; 540/512.000; 540/523.000

L10 ANSWER 26 OF 32 USPATFULL

AN 93:48388 USPATFULL  
TI Soluble forms of low affinity Fc gamma receptors, process for their identification and dosage, a corresponding dosage kit, and applications  
IN Khayat, David, Paris, France  
Unkeless, Jay, Brooklyn, NY, United States  
Jacquillat, Claude, Paris, France  
PA Universite Pierre et Maire Curie, Paris, France (non-U.S. corporation)  
PI US 5219728 930615  
WO 8806733 880907  
AI US 89-353676 890407 (7)  
WO 88-FR103 880223  
890407 PCT 371 date  
890407 PCT 102(e) date

PRAI FR 87-2400 870224

DT Utility  
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Preston, David R.  
LREP Jacobson, Price, Holman & Stern  
CLMN Number of Claims: 24  
ECL Exemplary Claim: 1  
DRWN 8 Drawing Figure(s); 4 Drawing Page(s)  
LN.CNT 601

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Searcher : Shears 308-4994

AB Receptors, characterized by the fact that they consist of the product obtained by affinity chromatography on a column coupled with 3 G8 antibodies or lectins or polyclonal anti-receptor FcR antibodies of a biological fluid of human origin, then by gel permeation. The spectrum of said product, electrophoresis acrylamide gel in reducing condition, comprising a major band corresponding to a molecular mass of between 72000 and 76000 daltons, and a number of minor bands. According to its purified form, the receptor consists of a glycoprotein with a molecular mass of between 72000 and 76000 daltons, recognized by ELISA and Western Blotting by the **monoclonal** anti-Leu 11b antibody. Application of said receptors to diagnosis and to follow-up treatment of diseases involving Fc receptors (infectious diseases, diseases of the autoimmune system, rejection of transplants, cancer and myeloma and AIDS), as well as to the study of human polymorphisms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/007.200  
 INCLS: 530/380.000; 530/395.000; 435/007.900; 435/007.920;  
 435/007.940; 435/007.950; 514/002.000; 514/008.000  
 NCL NCLM: 435/007.200  
 NCLS: 435/007.900; 435/007.920; 435/007.940; 435/007.950;  
 514/002.000; 514/008.000; 530/380.000; 530/395.000

L10 ANSWER 27 OF 32 USPATFULL

AN 91:71212 USPATFULL  
 TI Methods for screening antibodies for use as immunotoxins  
 IN Uhr, Jonathan W., 12355 Montego Plz., Dallas, TX, United States  
 75230  
 Vitetta, Ellen S., 6914 Pemberton Dr., Dallas, TX, United States  
 75230  
 PA Board of Regents, Austin, TX, United States (U.S. corporation)  
 PI US 5045451 910903  
 AI US 88-262974 881026 (7)  
 DT Utility  
 EXNAM Primary Examiner: Saunders, David A.  
 CLMN Number of Claims: 10  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Figure(s); 1 Drawing Page(s)  
 LN.CNT 671

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present disclosure described an assay for screening **monoclonal** antibodies for their potential as highly cytotoxic immunotoxins. The assay involves treating cells with dilutions of the test antibody followed by a Fab fragment of a secondary antibody coupled to an A chain toxin ("indirect assay"). The cytotoxicity of the indirect assay is compared to that of the direct assay where the **monoclonal** antibody is coupled to

Searcher : Shears 308-4994

an A chain toxin. Indirect and direct assays were carried out using 14 antibodies and a panel of 8 human and mouse cell types. The two assays showed virtually 100% correlation. The indirect assay, therefore, predicts the potency of a given **monoclonal** antibody to make an effective immunotoxin and should be useful in screening **monoclonal** antibodies for use as immunotoxins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/007.230  
 INCLS: 435/029.000; 435/007.240; 436/503.000; 436/512.000;  
 436/519.000; 436/547.000; 436/548.000; 436/813.000  
 NCL NCLM: 435/007.230  
 NCLS: 435/007.240; 435/029.000; 436/503.000; 436/512.000;  
 436/519.000; 436/547.000; 436/548.000; 436/813.000

L10 ANSWER 28 OF 32 USPATFULL  
 AN 90:61235 USPATFULL  
 TI Hepatic blocking agents  
 IN Baldwin, Robert W., Long Eaton, England  
 Byers, Vera S., San Francisco, CA, United States  
 PA Xoma Corporation, Berkeley, CA, United States (U.S. corporation)  
 PI US 4946675 900807  
 AI US 87-55266 870527 (7)  
 DT Utility  
 EXNAM Primary Examiner: Draper, Garnette  
 LREP Townsend and Townsend  
 CLMN Number of Claims: 10  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 607

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel methods and compositions are provided for the enhancement of the biodistribution of immunoconjugates useful in the diagnosis and treatment of a variety of conditions including cancer in many of its forms. The compositions of the present invention provide for enhanced bioavailability of immunoconjugates for the most part by blocking mammalian cell surface receptors present on cells of the reticuloendothelial system, especially in tissues responsible for the elimination of waste products and blood filtration. Such tissues include the liver, spleen, and kidneys. The compositions are administered in conjunction with an immunoconjugate in a pharmaceutically acceptable vehicle and may be provided in kits for convenient administration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/085.910  
 INCLS: 514/002.000; 514/008.000; 514/023.000; 514/059.000;  
 514/885.000; 530/389.000; 530/391.000; 435/007.000;  
 Searcher : Shears 308-4994

435/810.000; 436/543.000  
 NCL NCLM: 424/182.100  
 NCLS: 435/007.230; 435/810.000; 436/543.000; 514/002.000;  
 514/008.000; 514/023.000; 514/059.000; 514/885.000;  
 530/391.700; 530/391.900

L10 ANSWER 29 OF 32 USPATFULL

AN 89:15167 USPATFULL

TI Stable formulations of ricin toxin a chain and of  
 RTA-immunoconjugates and stabilizer screening methods therefor

IN Ferris, Robert, Walnut Creek, CA, United States

PA Cetus Corporation, Emeryville, CA, United States (U.S.  
 corporation)

PI US 4808705 890228

AI US 86-944347 861219 (6)

DT Utility

EXNAM Primary Examiner: Phillips, Delbert R.; Assistant Examiner:  
 Draper, Garnette D.

LREP Lauder, Leona L.; Halluin, Albert P.; Giotto, Gregory J.

CLMN Number of Claims: 46

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 937

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Highly stable pharmaceutical compositions suitable for parenteral  
 administration to animals or humans comprising a therapeutically  
 effective amount of an RTA-immunoconjugate dissolved in an inert  
 carrier method comprising a stabilizer are claimed. Screening  
 methods for selecting stabilizers effective in preventing  
 precipitation and aggregation of such compositions are described.  
 Preferred stabilizers includes glycerol at a concentration (v/v)  
 of from about 25 to about 35%; dextran sulfates having molecular  
 weights from about 0.1.times.10.sup.6 to about 2.times.10.sup.6  
 daltons; and human serum albumin.

The invention further comprises such compositions which have been  
 lyophilized and/or reconstituted wherein the stabilizer is  
 non-volatile, and may further comprise a carbohydrate stabilizer.

The invention further comprises stabilized RTA compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/391.000

INCLS: 530/390.000; 530/808.000; 530/370.000; 424/085.910;  
 514/002.000; 514/885.000; 514/008.000

NCL NCLM: 424/183.100

NCLS: 424/278.100; 514/002.000; 514/008.000; 514/885.000;  
 530/370.000; 530/391.700; 530/808.000; 530/861.000

L10 ANSWER 30 OF 32 USPATFULL  
 AN 88:82113 USPATFULL  
 TI Anti-immunoglobulin toxin conjugates useful in the treatment of B cell tumors  
 IN Uhr, Jonathan W., Dallas, TX, United States  
 Vitetta, Ellen S., Dallas, TX, United States  
 PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)  
 PI US 4792447 881220  
 AI US 83-498754 830527 (6)  
 RLI Continuation-in-part of Ser. No. US 81-286090, filed on 23 Jul 1981, now abandoned  
 DT Utility  
 EXNAM Primary Examiner: Hazel, Blondel  
 LREP Arnold, White & Durkee  
 CLMN Number of Claims: 8  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 893  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB Highly specific antibodies directed against immunoglobulin determinants coupled to one or more toxin molecules provide antibody-toxin conjugates which are useful in selectively inhibiting the growth of target immunoglobulin generating cells. The antibody-toxin conjugate consists of an antibody specific for a selected immunoglobulin determinant including isotypic, allotypic or idiotypic variable determinants, coupled to one or more toxin molecules. Anti-idiotypic toxin conjugates are provided which have specificity which distinguishes B cell tumor cells from normal B cells. Also disclosed is an antibody-toxin conjugate consisting of anti-IgD A chain. The antibody-toxin conjugate is used as a cell or tumor specific cytotoxic agent directed selectively against those cells expressing the corresponding immunoglobulin to which the antibody portion has specificity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 INCL INCLM: 424/085.910  
 INCLS: 530/387.000  
 NCL NCLM: 424/183.100  
 NCLS: 424/805.000; 424/809.000; 530/387.200; 530/388.730;  
 530/391.700; 530/862.000; 530/864.000; 530/866.000

L10 ANSWER 31 OF 32 USPATFULL  
 AN 83:1740 USPATFULL  
 TI Protein hybrid having cytotoxicity and process for the preparation thereof  
 IN Masuho, Yasuhiko, Hino, Japan  
 Hara, Takeshi, Hachioji, Japan  
 PA Teijin Limited, Osaka, Japan (non-U.S. corporation)  
 Searcher : Shears 308-4994

PI US 4368149 830111  
AI US 81-331342 811216 (6)  
PRAI JP 80-180553 801222  
DT Utility  
EXNAM Primary Examiner: Schain, Howard E.  
LREP Sughrue, Mion, Zinn, Macpeak & Seas  
CLMN Number of Claims: 7  
ECL Exemplary Claim: 1  
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 689

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A protein hybrid having cytotoxicity obtained by covalently bonding an immunoglobulin or its fragment, which is capable of binding selectively to an antigen possessed by a cell to be destroyed, to a protein, which is obtained from Momordica charantia and has an activity to terminate protein synthesis. This protein hybrid displays remarkable cytotoxicity against target cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 260/112.000B  
INCLS: 424/085.000; 424/088.000  
NCL NCLM: 530/391.900  
NCLS: 424/179.100; 424/184.100; 530/389.600; 530/391.700;  
530/866.000

L10 ANSWER 32 OF 32 USPATFULL

AN 82:60306 USPATFULL  
TI Cytotoxic protein hybrid and process for the preparation thereof  
IN Masuho, Yasuhiko, Hino, Japan  
Kishida, Kazuo, Hino, Japan  
Hara, Takeshi, Hachioji, Japan  
PA Teijin Limited, Osaka, Japan (non-U.S. corporation)  
PI US 4363758 821214  
AI US 81-331347 811216 (6)  
PRAI JP 80-180552 801222  
DT Utility  
EXNAM Primary Examiner: Schain, Howard E.  
LREP Sughrue, Mion, Zinn, Macpeak & Seas  
CLMN Number of Claims: 7  
ECL Exemplary Claim: 1  
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)  
LN.CNT 693

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A cytotoxic protein hybrid obtained by covalently bonding an immunoglobulin or its fragment, which is capable of linking selectively with an antigen possessed by a cell to be destroyed, to a protein, which is obtained from Phytolacca americana and has an activity to terminate protein synthesis. This protein hybrid

Searcher : Shears 308-4994



08/905293

displays remarkable cytotoxicity against target cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 260/112.000B

INCLS: 424/085.000; 424/088.000

NCL NCLM: 530/391.900

NCLS: 424/179.100; 424/183.100; 530/370.000; 530/379.000;  
530/389.600; 530/391.700; 530/866.000

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FILE COVERS 1967 - 7 Dec 1998 VOL 129 ISS 24

FILE LAST UPDATED: 7 Dec 1998 (981207/ED)

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L1 3645 SEA FILE=REGISTRY ABB=ON PLU=ON IMMUNOGLOBULIN ?/CN  
L11 115196 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR IMMUNOGLOBULIN OR  
IMMUNO GLOBULIN OR IG#  
L12 459 SEA FILE=CAPLUS ABB=ON PLU=ON L11(S)TOXIC?  
L13 43 SEA FILE=CAPLUS ABB=ON PLU=ON L12(S)INHIBIT?  
L14 7 SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (LEX OR LEY OR  
LE OR BR96 OR (BR OR CHIBR OR HBR) (W)96 OR CHIBR96 OR  
HBR96 OR HB10460 OR HB10036 OR HB(W) (10460 OR 10036) OR  
MOAB OR MAB OR MONOCLON? OR HYBRIDOMA)

=> s l14 not l5

L15 3 L14 NOT L5

=> d 1-3 .bevstr

Searcher : Shears 308-4994

L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 1998 ACS  
 AN 1992:649799 CAPLUS  
 DN 117:249799  
 TI Selection of an escape variant of *Borrelia burgdorferi* by use of bactericidal **monoclonal** antibodies to OspB  
 AU Coleman, James L.; Rogers, Rene C.; Benach, Jorge L.  
 CS State of New York Dep. Health, Stony Brook, NY, 11794-8692, USA  
 SO Infect. Immun. (1992), 60(8), 3098-104  
 CODEN: INFIBR; ISSN: 0019-9567  
 DT Journal  
 LA English  
 AB Two IgG **monoclonal** antibodies (**MABs**) to outer surface protein B (OspB) (CB2 and CB6), affinity purified from mouse ascitic fluid, exhibited concn.-dependent inhibitory and bactericidal properties against *B. burgdorferi* after a 24-h incubation period in spirochete medium. Fab fragments derived from these **MABs** showed the same effects, indicating that they were not caused by agglutination of the organisms by the intact **MABs**. The inhibition of spirochete growth in cultures contg. **MABs** was also detected by spectrophotometric anal. of the media. CB2 did not inhibit the growth of *B. hermsii* or the BEP4 strain of *B. burgdorferi*, neither of which is recognized by the **MAB**. Affinity-purified IgG from **hybridoma** supernatants had similar effects on *B. burgdorferi* as the ascitic-fluid-derived IgG did, indicating that the **inhibitory** and bactericidal properties were not due to nonspecific **toxic** contaminants. The bactericidal properties of the **MABs** were not complement-dependent. SDS-PAGE anal. of *B. burgdorferi* organisms surviving after exposure to CB2 revealed an escape variant which failed to express OspB. The continued presence of OspA in these escape variants indicates that the lack of OspB was not due to the loss of the plasmid which contains the genes for both of these proteins.

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 1998 ACS  
 AN 1992:542983 CAPLUS  
 DN 117:142983  
 TI **Inhibition** of hematopoietic tumor growth by combined treatment with deferoxamine and an IgG **monoclonal** antibody against the transferrin receptor: evidence for a threshold model of iron deprivation **toxicity**  
 AU Kemp, John D.; Thorson, John A.; Stewart, Barbara C.; Naumann, Paul W.  
 CS Coll. Med., Univ. Iowa, Iowa City, IA, 52242, USA  
 SO Cancer Res. (1992), 52(15), 4144-8  
 CODEN: CNREA8; ISSN: 0008-5472  
 DT Journal

Searcher : Shears 308-4994

LA English

AB Recent studies have suggested that iron deprivation may represent a useful new approach in cancer therapy, and several strategies for producing such deprivation are now under investigation. The authors recently provided evidence that combined treatment with the iron chelator deferoxamine and an IgG **monoclonal** antibody against the transferrin receptor (ATRA) produces synergistic inhibition of hematopoietic tumor cell growth in vitro (J. D. Kemp, K. M. Smith, L. J. Kanner et al., 1900). The current study is an attempt to analyze the mechanisms responsible for the synergistic interaction. The data show that a single IgG ATRA can produce up to 75% inhibition of iron uptake while having little effect on DNA synthesis; this suggests that tumor cells either take up or have stored amts. of iron well in excess of that required to support immediate metabolic needs. When deferoxamine and the IgG ATRA are used together, the effects on iron acquisition and receptor down-modulation are either additive or subadditive but are clearly not synergistic. Overall, the findings suggest that the IgG ATRA produces an injury to iron uptake that is just below a crit. threshold and that the addnl. effect provided by the iron chelator is sufficient to exceed that threshold and produce a rapid depletion of iron pools that are vital for short-term DAN synthesis. IgG ATRAS thus seem to be of even greater interest as therapeutic reagents, and further study of their properties and of how they interact with deferoxamine appears to be warranted.

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 1998 ACS

AN 1983:105510 CAPLUS

DN 98:105510

TI **Monoclonal** antibody and an antibody-toxin conjugate to a cell surface proteoglycan of melanoma cells suppress in vivo tumor growth

AU Bumol, T. F.; Wang, Q. C.; Reisfeld, R. A.; Kaplan, N. O.

CS Dep. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA

SO Proc. Natl. Acad. Sci. U. S. A. (1983), 80(2), 529-33

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB A **monoclonal** antibody directed against a cell surface chondroitin sulfate proteoglycan of human melanoma cells, 9.2.27, and its diphtheria toxin A chain (DTA) conjugate were investigated for their effects on in vitro protein synthesis and in vivo tumor growth of human melanoma cells. The 9.2.27 IgG and its DTA conjugate display similar serol. activities against melanoma target cells but only the conjugate can induce consistent in vitro **inhibition** of protein synthesis and **toxicity** in M21 melanoma cells. However, both 9.2.27 IgG and its DTA conjugate induce suppression of M21 tumor growth in vivo in an immunotherapy model of a rapidly growing tumor in athymic nu/nu mice, suggesting

Searcher : Shears 308-4994

08/905293

that other host mechanisms may mediate monoclonal antibody-induced tumor suppression.

=> d his 120-; d 1-21 .bevpat

(FILE 'USPATFULL' ENTERED AT 16:31:58 ON 07 DEC 1998)

L16 93 S L14  
L17 12 S L16 AND FUS? PROTEIN  
L18 83 S L16 AND ADMIN?  
L20 135 S L13  
L21 92 S L20 AND (BR96 OR (BR OR CHIBR OR HBR) (W) 96 OR CHIBR96 OR HBR) (W) 96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR HB(W) (10460 OR 10036) OR MOAB OR MAB OR MONOCLON? OR HYBRIDOMA)  
L22 1 S L21 AND (LEY OR LEX OR LE)  
L23 27 S L18 AND (IMMUNOTHERAP? OR IMMUN? THERAP?)  
L24 21 S (L22 OR L23) NOT L10

L24 ANSWER 1 OF 21 USPATFULL

AN 1998:128265 USPATFULL

TI Substituted amino alcohol compounds

IN Klein, J. Peter, Vashon, WA, United States  
Underiner, Gail E., Brier, WA, United States  
Kumar, Anil M., Seattle, WA, United States

PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)

PI US 5824677 981020

AI US 95-474816 950607 (8)

RLI Division of Ser. No. US 94-303842, filed on 8 Sep 1994, now patented, Pat. No. US 5641783 which is a continuation-in-part of Ser. No. US 93-152650, filed on 12 Nov 1993, now patented, Pat. No. US 5801181 And Ser. No. US 93-164081, filed on 8 Dec 1993, now patented, Pat. No. US 5470878, said Ser. No. US -152650 And Ser. No. US -164081, each Ser. No. US - which is a continuation-in-part of Ser. No. US 93-40820, filed on 31 Mar 1993, now abandoned

DT Utility

EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Cebulak, Mary C.

LREP McDermott, Will & Emery; Faciszewski, Esq., Stephen

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN 120 Drawing Figure(s); 89 Drawing Page(s)

LN.CNT 3136

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds having a straight or branched aliphatic hydrocarbon structure of formula I: ##STR1## In formula I, n is an integer from one to four and m is an integer from four to twenty.

Searcher : Shears 308-4994

Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or branched chain alkyl, alkenyl or alkynyl of up to twenty carbon atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8 alkoxy group or a substituted or unsubstituted carbocycle or heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a substituted or unsubstituted, saturated or unsaturated heterocycle having from four to eight carbon atoms, N being a hetero atom of the resulting heterocycle. R.sub.3 may be either hydrogen or C.sub.13. In the compounds, a total sum of carbon atoms comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and (CH.sub.2).sub.m does not exceed forty. R.sub.4 is a heterocycle comprising a substituted or unsubstituted, oxidized or reduced ring system, the ring system having a single ring or two to three fused rings, a ring comprising from three to seven ring atoms. The disclosed compounds are effective agents to inhibit undesirable responses to cell stimuli.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/222.500

INCLS: 514/223.500; 514/224.500; 514/226.800; 514/227.500;  
 514/228.800; 514/229.200; 514/230.500; 514/230.800;  
 514/237.800; 514/248.000; 514/249.000; 514/255.000;  
 514/258.000; 514/274.000; 514/301.000; 514/303.000;  
 514/311.000; 514/351.000; 514/360.000; 514/361.000;  
 514/362.000; 514/363.000; 514/364.000; 514/365.000;  
 514/367.000; 514/372.000; 514/373.000; 514/374.000;  
 514/375.000; 514/376.000; 514/378.000; 514/379.000;  
 514/380.000; 514/387.000; 514/395.000; 514/415.000;  
 514/418.000; 514/424.000; 514/425.000; 514/433.000;  
 514/452.000; 514/432.000; 514/438.000; 346/113.000;  
 346/114.000; 346/164.000; 346/300.000; 549/014.000;  
 549/050.000; 549/075.000; 549/367.000; 549/368.000;  
 544/002.000; 544/003.000; 544/005.000; 544/008.000;  
 544/053.000; 544/063.000; 544/065.000; 544/066.000;  
 544/067.000; 544/090.000; 544/091.000; 544/127.000;  
 544/128.000; 544/162.000; 544/215.000; 544/219.000;  
 544/229.000; 544/235.000; 544/237.000; 544/255.000;  
 544/278.000; 544/311.000; 544/353.000; 544/385.000;  
 548/123.000; 548/125.000; 548/131.000; 548/134.000;  
 548/143.000; 548/146.000; 548/153.000; 548/174.000;  
 548/207.000; 548/214.000; 548/215.000; 548/217.000;  
 548/221.000; 548/228.000; 548/229.000; 548/237.000;  
 548/240.000; 548/241.000; 548/243.000; 548/247.000;  
 548/267.200; 548/303.700; 548/307.100; 548/453.000;  
 548/486.000; 548/543.000; 548/546.000

NCL NCLM: 514/222.500

NCLS: 514/223.500; 514/224.500; 514/226.800; 514/227.500;

Searcher : Shears 308-4994

514/228.800; 514/229.200; 514/230.500; 514/230.800;  
 514/237.800; 514/248.000; 514/249.000; 514/255.000;  
 514/258.000; 514/274.000; 514/301.000; 514/303.000;  
 514/311.000; 514/351.000; 514/360.000; 514/361.000;  
 514/362.000; 514/363.000; 514/364.000; 514/365.000;  
 514/367.000; 514/372.000; 514/373.000; 514/374.000;  
 514/375.000; 514/376.000; 514/378.000; 514/379.000;  
 514/380.000; 514/387.000; 514/395.000; 514/415.000;  
 514/418.000; 514/424.000; 514/425.000; 514/432.000;  
 514/433.000; 514/438.000; 514/452.000; 544/002.000;  
 544/003.000; 544/005.000; 544/008.000; 544/053.000;  
 544/063.000; 544/065.000; 544/066.000; 544/067.000;  
 544/090.000; 544/091.000; 544/127.000; 544/128.000;  
 544/162.000; 544/215.000; 544/219.000; 544/229.000;  
 544/235.000; 544/237.000; 544/255.000; 544/278.000;  
 544/311.000; 544/353.000; 544/385.000; 546/113.000;  
 546/114.000; 546/164.000; 546/300.000; 548/123.000;  
 548/125.000; 548/131.000; 548/134.000; 548/143.000;  
 548/146.000; 548/153.000; 548/174.000; 548/207.000;  
 548/214.000; 548/215.000; 548/217.000; 548/221.000;  
 548/228.000; 548/229.000; 548/237.000; 548/240.000;  
 548/241.000; 548/243.000; 548/247.000; 548/267.200;  
 548/303.700; 548/307.100; 548/453.000; 548/486.000;  
 548/543.000; 548/546.000; 549/014.000; 549/050.000;  
 549/075.000; 549/367.000; 549/368.000

L24 ANSWER 2 OF 21 USPATFULL

AN 1998:128236 USPATFULL

TI Rnase-cv (coriolus versicolor)

IN Yang, Mable M. P., Block, 17B, fourth Fl., Baguio Villa, Hong Kong  
 Chen, George, Block, 17B, fourth Fl., Baguio Villa, Hong Kong

PI US 5824648 981020

AI US 94-359222 941219 (8)

RLI Continuation-in-part of Ser. No. US 92-983238, filed on 30 Nov  
 1992, now patented, Pat. No. US 5374714

DT Utility

EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Mohamed,  
 Abdel A.

LREP Norris, Jerome J.

CLMN Number of Claims: 4

ECL Exemplary Claim: 1

DRWN 26 Drawing Figure(s); 17 Drawing Page(s)

LN.CNT 797

AB A method of obtaining a novel polypeptide from a crude extraction  
 product of polysaccharide peptide *Coriolus versicolor* comprising:  
 a) boiling a water soluble powder of polysaccharide peptide  
*Coriolus versicolor*; b) centrifuging a boiled product from step  
 a); c) filtering a centrifuged product from step b); d) purifying  
 a solution from step c) by gel filtration chromatography; e)

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subjecting the purified material from step d) to HPLC using a reversed-phase at ambient temperature, f) subjecting the purified material from step e) to capillary isoelectrophoresis focusing; g) further purifying this product by HPLC and ionic exchange columns and h) purifying a protein by SDS-PAGE and i) recovering a peptide from 12 Kd to 16 kD. The peptide has the partial amino acid sequence GTAAAKEFERQHM SEQ ID NO:1.

INCL INCLM: 514/014.000  
 INCLS: 514/008.000; 514/012.000; 530/322.000; 530/324.000;  
 530/327.000; 530/350.000; 530/371.000; 530/395.000;  
 530/523.000; 536/123.100  
 NCL NCLM: 514/014.000  
 NCLS: 514/008.000; 514/012.000; 530/322.000; 530/324.000;  
 530/327.000; 530/350.000; 530/371.000; 530/395.000;  
 530/823.000; 536/123.100

L24 ANSWER 3 OF 21 USPATFULL

AN 1998:95236 USPATFULL

TI Mutant diphtheria toxin conjugates

IN Johnson, Virginia G., College Park, MD, United States  
 Greenfield, Larry, Emeryville, CA, United States  
 Youle, Richard J., Garrett Park, MD, United States  
 Laird, Walter, Pinole, CA, United States

PA The United States of America as represented by the Department of  
 Health and Human Services, Washington, DC, United States (U.S.  
 government)  
 Cetus Corporation, Emeryville, CA, United States (U.S.  
 corporation)

PI US 5792458 980811

AI US 94-323591 941017 (8)

RLI Continuation of Ser. No. US 92-934250, filed on 25 Aug 1992, now  
 abandoned which is a division of Ser. No. US 89-301376, filed on  
 25 Jan 1989, now patented, Pat. No. US 5208021 which is a division  
 of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned  
 which is a continuation-in-part of Ser. No. US 87-105172, filed on  
 5 Oct 1987, now abandoned

DT Utility

EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Lucas,  
 John

LREP Klarquist Sparkman Campbell Leigh & Whinston

CLMN Number of Claims: 39

ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 9 Drawing Page(s)

LN.CNT 1444

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A potent and specific immunotoxin is prepared by coupling an  
 inactivated diphtheria toxin to a binding moiety such as a  
 monoclonal antibody or transferrin. The immunotoxins are

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specific for human tumors and leukemias and are indistinguishable in cell toxicity from that of the native toxin linked to the binding domain without the toxicity to other cells. The immunotoxin is useful in treating graft versus host disease as well as selectively killing tumor cells, such as medulloblastoma and glioblastoma cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/183.100  
 INCLS: 424/155.100; 424/174.100; 424/094.100; 424/832.000;  
 514/012.000; 530/350.000; 530/387.700; 530/391.700  
 NCL NCLM: 424/183.100  
 NCLS: 424/094.100; 424/155.100; 424/174.100; 424/832.000;  
 514/012.000; 530/350.000; 530/387.700; 530/391.700

L24 ANSWER 4 OF 21 USPATFULL

AN 1998:91837 USPATFULL  
 TI Polyclonal antibody libraries  
 IN Sharon, Jacqueline, Chestnut Hill, MA, United States  
 PA The Trustees of Boston University, Boston, MA, United States (U.S. corporation)  
 PI US 5789208 980804  
 AI US 97-802824 970219 (8)  
 RLI Continuation of Ser. No. US 94-189360, filed on 31 Jan 1994, now abandoned  
 DT Utility  
 EXNAM Primary Examiner: Chambers, Jasmine C.; Assistant Examiner: Priebe, Scott D.  
 LREP Eisenstein, Ronald I.  
 CLMN Number of Claims: 26  
 ECL Exemplary Claim: 1  
 DRWN 21 Drawing Figure(s); 14 Drawing Page(s)  
 LN.CNT 2370

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is directed to methods for the creation and use of libraries of proteins which comprise polyclonal antibodies to a common antigen or group of antigens, receptor proteins with related variable regions, or other immune related proteins with variable regions. These polyclonal antibody libraries can be used to treat or prevent diseases and disorders including neoplasia such as cancer and other malignancies, parasitic infections, bacterial infections, viral infections and disorders such as genetic defects and deficiencies. Protein libraries may be patient-specific, disease-specific or both patient- and disease-specific. Libraries can also be used to detect a disease or disorder in a patient either by direct imaging or through the use of a diagnostic kit. The invention further includes novel cloning methods for the creation and transfer of nucleic acid sequences encoding protein variable regions and novel cloning

Searcher : Shears 308-4994



vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/091.410  
 INCLS: 435/006.000; 435/006.910; 435/091.400; 435/172.000;  
 435/320.100  
 NCL NCLM: 435/091.410  
 NCLS: 435/006.000; 435/069.100; 435/091.400; 435/320.100;  
 435/488.000; 435/489.000

L24 ANSWER 5 OF 21 USPATFULL

AN 1998:79344 USPATFULL  
 TI Method for preparing substituted amino alcohol compounds  
 IN Klein, J. Peter, Vashon, WA, United States  
 Underiner, Gail E., Brier, WA, United States  
 Kumar, Anil M., Seattle, WA, United States  
 PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S.  
 corporation)  
 PI US 5777117 980707  
 AI US 95-472569 950607 (8)  
 RLI Division of Ser. No. US 94-303842, filed on 8 Sep 1994 which is a  
 continuation-in-part of Ser. No. US 93-152650, filed on 12 Nov  
 1993 And Ser. No. US 93-164081, filed on 8 Dec 1993 which is a  
 continuation-in-part of Ser. No. US 93-40820, filed on 31 Mar  
 1993, now abandoned, said Ser. No. US -152650 which is a  
 continuation-in-part of Ser. No. US -40820  
 DT Utility  
 EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Cebulak, Mary  
 C.  
 LREP McDermott, Will & Emery  
 CLMN Number of Claims: 22  
 ECL Exemplary Claim: 1  
 DRWN 118 Drawing Figure(s); 92 Drawing Page(s)  
 LN.CNT 3153

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a process for preparing compounds having a straight  
 or branched aliphatic hydrocarbon structure of formula I: ##STR1##  
 In formula I, n is an integer from one to four and m is an integer  
 from four to twenty. Independently, R.sub.1 and R.sub.2 are  
 hydrogen, a straight or branched chain alkyl, alkenyl or alkynyl  
 of up to twenty carbon atoms in length or --(CH.sub.2).sub.w  
 R.sub.5. If R.sub.1 or R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w  
 may be an integer from one to twenty and R.sub.5 may be an  
 hydroxyl, halo, C.sub.1-8 alkoxy group or a substituted or  
 unsubstituted carbocycle or heterocycle. Alternatively, R.sub.1  
 and R.sub.2 may jointly form a substituted or unsubstituted,  
 saturated or unsaturated heterocycle having from four to eight  
 carbon atoms, N being a hetero atom of the resulting heterocycle.  
 R.sub.3 may be either hydrogen or C.sub.1-3. In the compounds, a

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total sum of carbon atoms comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and (CH.sub.2).sub.m does not exceed forty. R.sub.4 is a terminal moiety comprising a substituted or unsubstituted, oxidized or reduced ring system, the ring system having a single ring or two to three fused rings, a ring comprising from three to seven ring atoms. The disclosed compounds are effective agents to inhibit undesirable responses to cell stimuli.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 544/267.000  
 INCLS: 544/257.000; 544/285.000; 544/286.000; 544/287.000;  
 544/311.000; 546/141.000; 546/243.000; 546/246.000;  
 548/477.000; 548/546.000  
 NCL NCLM: 544/267.000  
 NCLS: 544/257.000; 544/285.000; 544/286.000; 544/287.000;  
 544/311.000; 546/141.000; 546/243.000; 546/246.000;  
 548/477.000; 548/546.000

L24 ANSWER 6 OF 21 USPATFULL

AN 1998:68822 USPATFULL  
 TI Cysteine-pegylated proteins  
 IN Braxton, Scott M., San Mateo, CA, United States  
 PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)  
 PI US 5766897 980616  
 AI US 95-427100 950421 (8)  
 RLI Continuation-in-part of Ser. No. US 93-144758, filed on 29 Oct 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-924294, filed on 3 Aug 1992, now patented, Pat. No. US 5457090 which is a continuation of Ser. No. US 90-542484, filed on 21 Jun 1990, now patented, Pat. No. US 5187089, issued on 16 Feb 1993  
 DT Utility  
 EXNAM Primary Examiner: Hendricks, Keith D.; Assistant Examiner: Hobbs, Lisa J.  
 LREP Fish & Richardson P.C.  
 CLMN Number of Claims: 10  
 ECL Exemplary Claim: 1  
 DRWN 7 Drawing Figure(s); 7 Drawing Page(s)  
 LN.CNT 2765

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for the production of PEGylated proteins having polyethylene glycol covalently bound to a cysteine residue present in either the naturally-occurring protein or introduced by site-specific mutation. Where the cysteine residue is introduced by mutation, the site for mutation is selected on the basis of the presence of an N-linked glycosylation site or the position of the residue which is normally solvent-accessible in the naturally-occurring protein.

Searcher : Shears 308-4994

The modified proteins produced by the method of the invention are referred to as cysteine-PEGylated proteins. Proteins PEGylated according to the invention have increased half-lives following administration to a subject and decreased immunogenicity and antigenicity, while retaining substantially the same level of biological activity as that of the naturally-occurring, unmodified protein. Modification of proteins according to methods of the invention thus provide improved pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/172.100  
INCLS: 435/188.000; 435/212.000; 435/219.000  
NCL NCLM: 435/463.000  
NCLS: 435/188.000; 435/212.000; 435/219.000

L24 ANSWER 7 OF 21 USPATFULL

AN 1998:64728 USPATFULL  
TI Combined treatment of iron depletion and IgG antibody  
IN Kemp, John D., Iowa City, IA, United States  
PA University of Iowa Research Foundation, Iowa City, IA, United States (U.S. corporation)  
PI US 5762932 980609  
AI US 96-718293 960920 (8)  
RLI Continuation of Ser. No. US 94-358389, filed on 19 Dec 1994, now abandoned which is a continuation-in-part of Ser. No. US 93-54679, filed on 29 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 90-514706, filed on 26 Apr 1990, now abandoned  
DT Utility  
EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Bansal, Geetha P.  
LREP Kohn & Associates  
CLMN Number of Claims: 1  
ECL Exemplary Claim: 1  
DRWN 13 Drawing Figure(s); 4 Drawing Page(s)  
LN.CNT 782

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of inhibiting tumor growth includes the steps of depleting intracellular iron levels of tumor cells to increase expression of cellular transferrin receptors in tumor cells and then exposing the tumor cells to monoclonal IgG anti-transferrin receptor antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/143.100  
INCLS: 424/144.100; 424/155.100; 424/156.100; 514/575.000; 514/626.000  
NCL NCLM: 424/143.100  
NCLS: 424/144.100; 424/155.100; 424/156.100; 514/575.000;

Searcher : Shears 308-4994

514/626.000

L24 ANSWER 8 OF 21 USPATFULL  
AN 1998:51651 USPATFULL  
TI Substituted amino alcohol compounds  
IN Klein, J. Peter, Vashon, WA, United States  
Underiner, Gail E., Brier, WA, United States  
Kumar, Anil M., Seattle, WA, United States  
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S.  
corporation)  
PI US 5750575 980512  
AI US 95-475721 950607 (8)  
RLI Division of Ser. No. US 94-303842, filed on 8 Sep 1994, now  
patented, Pat. No. US 5641783 which is a continuation-in-part of  
Ser. No. US 93-152650, filed on 12 Nov 1993 And a  
continuation-in-part of Ser. No. US 93-164081, filed on 8 Dec  
1993, now patented, Pat. No. US 5470878 which is a  
continuation-in-part of Ser. No. US 93-40820, filed on 31 Mar  
1993, now abandoned  
DT Utility  
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Cebulak, M.  
LREP McDermott, Will & Emery; Faciszewski, Esq., Stephen  
CLMN Number of Claims: 18  
ECL Exemplary Claim: 1  
DRWN 115 Drawing Figure(s); 90 Drawing Page(s)  
LN.CNT 3115  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Disclosed are compounds having a straight or branched aliphatic  
hydrocarbon structure of formula I: ##STR1## In formula I, n is an  
integer from one to four and m is an integer from four to twenty.  
Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or  
branched chain alkyl, alkenyl or alkynyl of up to twenty carbon  
atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or  
R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from  
one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8  
alkoxyl group or a substituted or unsubstituted carbocycle or  
heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a  
substituted or unsubstituted, saturated or unsaturated heterocycle  
having from four to eight carbon atoms, N being a hetero atom of  
the resulting heterocycle. R.sub.3 may be either hydrogen or  
C.sub.1-3. In the compounds, a total sum of carbon atoms  
comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and  
(CH.sub.2).sub.m does not exceed forty. R.sub.4 is a carbocycle  
comprising a substituted or unsubstituted ring system, the ring  
system having a single ring or two fused rings, a ring comprising  
from three to seven ring atoms. The disclosed compounds are  
effective agents to inhibit undesirable responses to cell stimuli.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Searcher : Shears 308-4994

INCL INCLM: 514/617.000  
 INCLS: 514/653.000; 564/182.000; 564/355.000; 564/361.000  
 NCL NCLM: 514/617.000  
 NCLS: 514/653.000; 564/182.000; 564/355.000; 564/361.000

L24 ANSWER 9 OF 21 USPATFULL

AN 1998:27768 USPATFULL

TI Treatment of tumors of the central nervous system with immunotoxins

IN Johnson, Virginia, College Park, MD, United States

Youle, Richard J., Chevy Chase, MD, United States

PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)

PI US 5728383 980317

AI US 94-258712 940613 (8)

RLI Continuation of Ser. No. US 92-925417, filed on 10 Aug 1992, now patented, Pat. No. US 5352447 which is a continuation of Ser. No. US 89-401412, filed on 1 Sep 1989, now abandoned which is a continuation-in-part of Ser. No. US 89-301376, filed on 25 Jan 1989, now patented, Pat. No. US 5208021 which is a division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned

DT Utility

EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Bakalyar, Heather A.

LREP Klarquist, Sparkman, Campbell, Leigh & Whinston

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN 11 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 1097

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Potent and specific immunotoxins are prepared by conjugation of moieties binding to receptors on the surface of tumor cells to a mutant diphtheria toxin having A-chain translocation activity, but lacking membrane-binding activity. The immunotoxins are used to treat primary tumors of neurologic origin, metastatic tumors of small cell lung carcinoma or breast carcinoma origin, leptomeningeal leukemia and leptomeningeal carcinomatosis. The preferred route of administration of the immunotoxin is to a compartment of the body containing cerebrospinal fluid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/183.100

INCLS: 424/832.000; 424/194.100; 424/195.110; 514/008.000;  
 514/012.000; 514/021.000; 530/391.700; 530/394.000;  
 530/380.000; 530/388.100; 530/388.200; 530/388.220;  
 530/387.700; 530/388.800; 530/363.000

Searcher : Shears 308-4994

NCL NCLM: 424/183.100  
NCLS: 424/194.100; 424/195.110; 424/832.000; 514/008.000;  
514/012.000; 514/021.000; 530/363.000; 530/380.000;  
530/387.700; 530/388.100; 530/388.200; 530/388.220;  
530/388.800; 530/391.700; 530/394.000

L24 ANSWER 10 OF 21 USPATFULL  
AN 97:54233 USPATFULL  
TI Substituted amino alcohol compounds  
IN Klein, J. Peter, Vashon, WA, United States  
Underiner, Gail E., Brier, WA, United States  
Kumar, Anil M., Seattle, WA, United States  
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S.  
corporation)  
PI US 5641783 970624  
AI US 94-303842 940908 (8)  
RLI Continuation-in-part of Ser. No. US 93-152650, filed on 12 Nov  
1993 And Ser. No. US 93-164081, filed on 8 Dec 1993, now patented,  
Pat. No. US 5470878  
DT Utility  
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner:  
Cebulak, Mary C.  
LREP Faciszewski, Stephen; Oster, Jeffrey B.  
CLMN Number of Claims: 22  
ECL Exemplary Claim: 1  
DRWN 115 Drawing Figure(s); 88 Drawing Page(s)  
LN.CNT 3206  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds having a straight or branched aliphatic  
hydrocarbon structure of formula I: ##STR1## In formula I, n is an  
integer from one to four and m is an integer from four to twenty.  
Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or  
branched chain alkyl, alkenyl or alkynyl of up to twenty carbon  
atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or  
R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from  
one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8  
alkoxyl group or a substituted or unsubstituted carbocycle or  
heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a  
substituted or unsubstituted, saturated or unsaturated heterocycle  
having from four to eight carbon atoms, N being a hetero atom of  
the resulting heterocycle. R.sub.3 may be either hydrogen or  
C.sub.1-3. In the compounds, a total sum of carbon atoms  
comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and  
(CH.sub.2).sub.m does not exceed forty. R.sub.4 is a terminal  
moiety comprising a substituted or unsubstituted, oxidized or  
reduced ring system, the ring system having a single ring or two  
to three fused rings, a ring comprising from three to seven ring  
atoms. The disclosed compounds are effective agents to inhibit  
undesirable responses to cell stimuli.

Searcher : Shears 308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/263.000

INCLS: 514/183.000; 514/222.500; 514/223.500; 514/224.200;  
514/226.800; 514/227.500; 514/228.800; 514/229.200;  
514/230.500; 514/230.800; 514/237.800; 514/241.000;  
514/242.000; 514/243.000; 514/246.000; 514/247.000;  
514/248.000; 514/249.000; 514/255.000; 514/256.000;  
514/258.000; 514/259.000; 514/261.000; 514/262.000;  
514/263.000; 514/270.000; 514/274.000; 514/297.000;  
514/300.000; 514/301.000; 514/302.000; 514/303.000;  
514/306.000; 514/307.000; 514/311.000; 514/312.000;  
514/315.000; 514/345.000; 514/351.000; 514/357.000;  
514/359.000; 514/360.000; 514/361.000; 514/362.000;  
514/363.000; 514/364.000; 514/365.000; 514/367.000;  
514/369.000; 514/372.000; 514/373.000; 514/374.000;  
514/375.000; 514/376.000; 514/378.000; 514/379.000;  
514/380.000; 514/381.000; 514/383.000; 514/389.000;  
514/394.000; 514/395.000; 514/398.000; 514/399.000;  
514/401.000; 514/404.000; 514/406.000; 514/413.000;  
514/415.000; 514/416.000; 514/418.000; 514/423.000;  
514/424.000; 514/425.000; 514/427.000; 514/428.000;  
544/001.000; 544/002.000; 544/003.000; 544/008.000;  
544/053.000; 544/063.000; 544/065.000; 544/066.000;  
544/067.000; 544/090.000; 544/091.000; 544/162.000;  
544/215.000; 544/216.000; 544/219.000; 544/220.000;  
544/224.000; 544/235.000; 544/239.000; 544/254.000;  
544/255.000; 544/257.000; 544/262.000; 544/272.000;  
544/277.000; 544/278.000; 544/280.000; 544/283.000;  
544/286.000; 544/301.000; 544/311.000; 544/335.000;  
544/336.000; 544/350.000; 544/353.000; 544/385.000;  
544/401.000; 546/102.000; 546/113.000; 546/114.000;  
546/115.000; 546/117.000; 546/118.000; 546/119.000;  
546/122.000; 546/138.000; 546/139.000; 546/150.000;  
546/153.000; 546/157.000; 546/164.000; 546/176.000;  
546/178.000; 546/242.000; 546/243.000; 546/246.000;  
546/264.000; 546/300.000; 546/334.000; 548/100.000;  
548/123.000; 548/125.000; 548/127.000; 548/128.000;  
548/131.000; 548/134.000; 548/146.000; 548/153.000;  
548/179.000; 548/186.000; 548/207.000; 548/214.000;  
548/215.000; 548/217.000; 548/221.000; 548/225.000;  
548/228.000; 548/229.000; 548/235.000; 548/237.000;  
548/240.000; 548/241.000; 548/243.000; 548/247.000;  
548/252.000; 548/267.200; 548/267.800; 548/303.700;  
548/306.400; 548/307.100; 548/309.700; 548/319.100;  
548/323.500; 548/340.100; 548/348.100; 548/349.100;  
548/356.100; 548/370.100; 548/375.100; 548/379.400;  
548/452.000; 548/453.000; 548/470.000; 548/482.000;  
548/485.000; 548/486.000; 548/491.000; 548/503.000;

Searcher : Shears 308-4994

08/905293

NCL NCLM: 548/532.000; 548/543.000; 548/546.000; 548/550.000;  
548/565.000; 548/566.000  
NCLS: 514/263.000  
514/183.000; 514/222.500; 514/223.500; 514/224.200;  
514/226.800; 514/227.500; 514/228.800; 514/229.200;  
514/230.500; 514/230.800; 514/237.800; 514/241.000;  
514/242.000; 514/243.000; 514/246.000; 514/247.000;  
514/248.000; 514/249.000; 514/255.000; 514/256.000;  
514/258.000; 514/259.000; 514/261.000; 514/262.000;  
514/270.000; 514/274.000; 514/297.000; 514/300.000;  
514/301.000; 514/302.000; 514/303.000; 514/306.000;  
514/307.000; 514/311.000; 514/312.000; 514/315.000;  
514/345.000; 514/351.000; 514/357.000; 514/359.000;  
514/360.000; 514/361.000; 514/362.000; 514/363.000;  
514/364.000; 514/365.000; 514/367.000; 514/369.000;  
514/372.000; 514/373.000; 514/374.000; 514/375.000;  
514/376.000; 514/378.000; 514/379.000; 514/380.000;  
514/381.000; 514/383.000; 514/389.000; 514/394.000;  
514/395.000; 514/398.000; 514/399.000; 514/401.000;  
514/404.000; 514/406.000; 514/413.000; 514/415.000;  
514/416.000; 514/418.000; 514/423.000; 514/424.000;  
514/425.000; 514/427.000; 514/428.000; 544/001.000;  
544/002.000; 544/003.000; 544/008.000; 544/053.000;  
544/063.000; 544/065.000; 544/066.000; 544/067.000;  
544/090.000; 544/091.000; 544/162.000; 544/215.000;  
544/216.000; 544/219.000; 544/220.000; 544/224.000;  
544/235.000; 544/239.000; 544/254.000; 544/255.000;  
544/257.000; 544/262.000; 544/272.000; 544/277.000;  
544/278.000; 544/280.000; 544/283.000; 544/286.000;  
544/301.000; 544/311.000; 544/335.000; 544/336.000;  
544/350.000; 544/353.000; 544/385.000; 544/401.000;  
546/102.000; 546/113.000; 546/114.000; 546/115.000;  
546/117.000; 546/118.000; 546/119.000; 546/122.000;  
546/138.000; 546/139.000; 546/150.000; 546/153.000;  
546/157.000; 546/164.000; 546/176.000; 546/178.000;  
546/242.000; 546/243.000; 546/246.000; 546/264.000;  
546/300.000; 546/334.000; 548/100.000; 548/123.000;  
548/125.000; 548/127.000; 548/128.000; 548/131.000;  
548/134.000; 548/146.000; 548/153.000; 548/179.000;  
548/186.000; 548/207.000; 548/214.000; 548/215.000;  
548/217.000; 548/221.000; 548/225.000; 548/228.000;  
548/229.000; 548/235.000; 548/237.000; 548/240.000;  
548/241.000; 548/243.000; 548/247.000; 548/252.000;  
548/267.200; 548/267.800; 548/303.700; 548/306.400;  
548/307.100; 548/309.700; 548/319.100; 548/323.500;  
548/340.100; 548/348.100; 548/349.100; 548/356.100;  
548/370.100; 548/375.100; 548/379.400; 548/452.000;  
548/453.000; 548/470.000; 548/482.000; 548/485.000;  
548/486.000; 548/491.000; 548/503.000; 548/532.000;

Searcher : Shears 308-4994



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548/543.000; 548/546.000; 548/550.000; 548/565.000;  
548/566.000

L24 ANSWER 11 OF 21 USPATFULL

AN 96:111463 USPATFULL

TI Enantiomerically pure hydroxylated xanthine compounds

IN Bianco, James A., Seattle, WA, United States

Woodson, Paul, Bothell, WA, United States

Porubek, David, Edmonds, WA, United States

Singer, Jack, Seattle, WA, United States

PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S.  
corporation)

PI US 5580874 961203

AI US 95-457685 950601 (8)

RLI Division of Ser. No. US 94-343810, filed on 22 Nov 1994, now  
abandoned which is a division of Ser. No. US 94-307554, filed on  
16 Sep 1994 which is a continuation of Ser. No. US 93-13977, filed  
on 4 Feb 1993, now abandoned which is a continuation-in-part of  
Ser. No. US 92-926665, filed on 7 Aug 1992, now abandoned which is  
a continuation-in-part of Ser. No. US 92-846354, filed on 4 Mar  
1992, now abandoned

DT Utility

EXNAM Primary Examiner: Criares, Theodore J.

LREP Faciszewski, Stephen

CLMN Number of Claims: 4

ECL Exemplary Claim: 1

DRWN 22 Drawing Figure(s); 22 Drawing Page(s)

LN.CNT 1733

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Them is disclosed compounds and pharmaceutical compositions that  
is R enantiomer of an .omega.-1 alcohol of a straight chain alkyl  
(C.sub.5-8) substituted at the 1-position of 3,7-disubstituted  
xanthine. The inventive compounds are effective in treating the  
side effects of immunosuppressive agent and interleukin-2 therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/263.000

NCL NCLM: 514/263.000

L24 ANSWER 12 OF 21 USPATFULL

AN 96:109072 USPATFULL

TI Methods and compositions concerning homogenous immunotoxin  
preparations

IN Ghetie, Victor F., Dallas, TX, United States

Uhr, Jonathan W., Dallas, TX, United States

Vitetta, Ellen S., Dallas, TX, United States

PA Board of Regents, The University of Texas, Austin, TX, United  
States (U.S. corporation)

PI US 5578706 961126

Searcher : Shears 308-4994

AI US 93-147768 931104 (8)  
 DT Utility  
 EXNAM Primary Examiner: Scheiner, Toni R.  
 LREP Arnold White & Durkee  
 CLMN Number of Claims: 8  
 ECL Exemplary Claim: 1  
 DRWN 9 Drawing Figure(s); 4 Drawing Page(s)  
 LN.CNT 1272

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunotoxin preparations are described in which the preparations are enriched for a single species of immunotoxin. Also described are methods for the preparation of the substantially purified immunotoxins (ITs). Also disclosed are methods for determining the most effective species of immunotoxin conjugates for treated diseases and pharmaceutical preparations for such treatments.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/391.700  
 INCLS: 530/391.100; 424/178.100; 424/183.100  
 NCL NCLM: 530/391.700  
 NCLS: 424/178.100; 424/183.100; 530/391.100

L24 ANSWER 13 OF 21 USPATFULL

AN 95:94924 USPATFULL  
 TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof  
 IN Calne, Roy, 22 Barrow Road, Cambridge, England CB2 2AS  
 PI US 5461058 951024  
 AI US 95-377163 950124 (8)  
 RLI Division of Ser. No. US 94-192648, filed on 7 Feb 1994, now patented, Pat. No. US 5403833, issued on 4 Apr 1995 which is a division of Ser. No. US 93-9570, filed on 26 Jan 1993, now patented, Pat. No. US 5308847 which is a division of Ser. No. US 91-738960, filed on 31 Jul 1991, now patented, Pat. No. US 5212155, issued on 18 May 1993 which is a division of Ser. No. US 89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899, issued on 31 Mar 1992  
 DT Utility  
 EXNAM Primary Examiner: Goldberg, Jerome D.  
 LREP Darby & Darby  
 CLMN Number of Claims: 10  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 425

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising administ ring to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of  
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inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/291.000

NCL NCLM: 514/291.000

L24 ANSWER 14 OF 21 USPATFULL

AN 95:29635 USPATFULL

TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof

IN Calne, Sir Roy, 22 Arrow Rd., Cambridge, England CB2 2AS

PI US 5403833 950404

AI US 94-192648 940207 (8)

RLI Division of Ser. No. US 93-9570, filed on 26 Jan 1993, now patented, Pat. No. US 5308847 which is a division of Ser. No. US 91-738960, filed on 31 Jul 1991, now patented, Pat. No. US 5212155, issued on 18 May 1993 which is a division of Ser. No. US 89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899, issued on 31 Mar 1992

DT Utility

EXNAM Primary Examiner: Goldberg, Jerome D.

LREP Darby & Darby

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 412

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/171.000

Searcher : Shears 308-4994

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INCLS: 514/291.000  
NCL NCLM: 514/171.000  
NCLS: 514/291.000

L24 ANSWER 15 OF 21 USPATFULL

AN 94:86179 USPATFULL

TI Immunotoxins for treatment of intracranial lesions and as adjunct to chemotherapy

IN Johnson, Virginia, College Park, MD, United States

Youle, Richard J., Garrett Park, MD, United States

PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)

PI US 5352447 941004

AI US 92-92541 920810 (7)

RLI Continuation of Ser. No. US 89-401412, filed on 1 Sep 1989, now abandoned which is a continuation-in-part of Ser. No. US 89-301376, filed on 25 Jan 1989, now patented, Pat. No. US 5208021 which is a division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned

DT Utility

EXNAM Primary Examiner: Kim, Kay K.

LREP Birch, Stewart, Kolasch & Birch

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN 11 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 1102

AB A potent and specific immunotoxin is prepared by coupling a binding-site inactivated diphtheria toxin (CRM 107) to a new binding moiety consisting of transferrin or a monoclonal antibody against the human transferrin receptor. These immunotoxins are tumor specific and lack the nonspecific toxicity produced by the binding activity of the native toxin. The immunotoxin is useful in treating primary brain tumors, metastatic tumors to the brain, CSF-borne tumors, leptomeningeal leukemia and leptomeningeal carcinomatosis.

INCL INCLM: 424/183.100

INCLS: 514/008.000; 514/012.000; 514/021.000; 530/391.700;  
530/394.000; 424/832.000

NCL NCLM: 424/183.100

NCLS: 424/832.000; 514/008.000; 514/012.000; 514/021.000;  
530/391.700; 530/394.000

L24 ANSWER 16 OF 21 USPATFULL

AN 94:37944 USPATFULL

TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof

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IN Calne, Sir Roy, 22 Arrow Rd., Cambridge, England CB2 2AS  
PI US 5308847 940503  
AI US 93-9570 930126 (8)  
RLI Division of Ser. No. US 91-738960, filed on 31 Jul 1991, now  
patented, Pat. No. US 5212155 which is a division of Ser. No. US  
89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899  
DT Utility  
EXNAM Primary Examiner: Goldberg, Jerome D.  
LREP Darby & Darby  
CLMN Number of Claims: 10  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 398

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method of inhibiting organ or tissue  
transplant rejection in a mammal in need thereof, comprising  
**administering** to said mammal a transplant rejection  
inhibiting amount of rapamycin. Also disclosed is a method of  
inhibiting organ or tissue transplant rejection in a mammal in  
need thereof, comprising **administering** to said mammal  
(a) an amount of rapamycin in combination with (b) an amount of  
one or more other chemotherapeutic agents for inhibiting  
transplant rejection, e.g., azathioprine, corticosteroids,  
cyclosporin and FK506, said amounts of (a) and (b) together being  
effective to inhibit transplant rejection and to maintain  
inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/262.000  
INCLS: 514/291.000  
NCL NCLM: 514/262.000  
NCLS: 514/291.000

L24 ANSWER 17 OF 21 USPATFULL

AN 93:39979 USPATFULL  
TI Methods of inhibiting transplant rejection in mammals using  
rapamycin and derivatives and prodrugs thereof  
IN Calne, Roy, Cambridge, England CB2 2AS  
PI US 5212155 930518  
AI US 91-738960 910731 (7)  
RLI Division of Ser. No. US 89-362354, filed on 6 Jun 1989, now  
patented, Pat. No. US 5100899  
DT Utility  
EXNAM Primary Examiner: Goldberg, Jerome D.  
LREP Darby & Darby  
CLMN Number of Claims: 10  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 396

Searcher : Shears 308-4994

08/905293

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising administering to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising administering to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/011.000  
INCLS: 514/291.000  
NCL NCLM: 514/011.000  
NCLS: 514/291.000

L24 ANSWER 18 OF 21 USPATFULL

AN 93:35474 USPATFULL  
TI Method of preparing diphtheria immunotoxins  
IN Johnson, Virginia G., College Park, MD, United States  
Greenfield, Larry, Emeryville, CA, United States  
Youle, Richard J., Garrett Park, MD, United States  
Laird, Walter, Pinole, CA, United States  
PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)  
Cetus Corporation, Emeryville, CA, United States (U.S. corporation)  
PI US 5208021 930504  
AI US 89-301376 890125 (7)  
RLI Division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned  
DT Utility  
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Mohamed, Abdel A.  
LREP Birch, Stewart, Kolasch & Birch  
CLMN Number of Claims: 14  
ECL Exemplary Claim: 1  
DRWN 14 Drawing Figure(s); 9 Drawing Page(s)  
LN.CNT 1266

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A potent and specific immunotoxin is prepared by coupling an inactivated diphtheria toxin to a binding moiety such as a monoclonal antibody or transferrin. The immunotoxins are

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specific for human tumors and leukemias and are indistinguishable in cell toxicity from that of the native toxin linked to the binding domain without the toxicity to other cells. The immunotoxin is useful in treating graft versus host disease as well as selectively killing tumor cells, such as medulloblastoma and glioblastoma cells.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/085.910  
 INCLS: 424/085.500; 424/085.800; 530/388.100; 530/388.220;  
 530/390.100; 530/409.000; 530/412.000; 530/417.000;  
 530/820.000; 435/069.100; 436/548.000

NCL NCLM: 530/391.900  
 NCLS: 424/085.500; 424/179.100; 435/069.100; 436/548.000;  
 530/300.000; 530/388.100; 530/388.220; 530/390.100;  
 530/394.000; 530/409.000; 530/412.000; 530/417.000;  
 530/820.000

## L24 ANSWER 19 OF 21 USPATFULL

AN 92:92536 USPATFULL  
 TI Methods and compositions for the treatment of Hodgkin's disease  
 IN Thorpe, Philip, Ruislip, United Kingdom  
 Engert, Andreas, London, United Kingdom  
 PA Imperial Cancer Research Technology, London, United Kingdom  
 (non-U.S. corporation)  
 PI US 5165923 921124  
 AI US 89-440050 891120 (7)  
 DT Utility  
 EXNAM Primary Examiner: Nucker, Christine; Assistant Examiner: Kim, Kay  
 K.  
 LREP Arnold, White & Durkee  
 CLMN Number of Claims: 29  
 ECL Exemplary Claim: 1  
 DRWN 9 Drawing Figure(s); 5 Drawing Page(s)  
 LN.CNT 2191

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods and compositions for the treatment of Hodgkin's disease and processes involving Hodgkin's disease cells or Reed-Sternberg cells, through specific elimination of Hodgkin's disease cells through the application of immunotoxin technology. The compositions of the invention include toxin conjugates composed of a Hodgkin's disease cell binding ligand conjugated to a toxin A chain moiety such as ricin A chain or deglycosylated ricin A chain, by means of a cross-linker or other conjugation which includes a disulfide bond. In preferred aspects of the invention, therapeutic amounts of conjugates composed of a CD-30 or IRac antibody or fragment thereof conjugated to deglycosylated A chain by means of an SMPT linker is administered to a Hodgkin's disease patient so as to specifically eliminate

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Hodgkin's disease cells without exerting significant toxicity against non-tumor cells. Also disclosed are particular **hybridomas** and **monoclonal** antibodies, and associated methodology, which may be employed, e.g., in the preparation of these immunotoxins as well as other uses such as diagnostic applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/085.910  
INCLS: 530/391.900; 530/388.700; 530/388.730; 530/388.750  
NCL NCLM: 424/179.100  
NCLS: 424/153.100; 424/154.100; 424/178.100; 530/388.700;  
530/388.730; 530/388.750; 530/391.900

L24 ANSWER 20 OF 21 USPATFULL

AN 92:25361 USPATFULL  
TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof  
IN Calne, Roy, 22 Arrow Road, Cambridge, England CB22AS  
PI US 5100899 920331  
AI US 89-362354 890606 (7)  
DT Utility  
EXNAM Primary Examiner: Goldberg, Jerome D.  
LREP Darby & Darby  
CLMN Number of Claims: 7  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 389

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/291.000  
NCL NCLM: 514/291.000

L24 ANSWER 21 OF 21 USPATFULL

AN 87:71534 USPATFULL  
TI Products and methods for treatment of cancer  
Searcher : Shears 308-4994



08/905293

IN Terman, David S., 25371 Outlook Dr., Carmel, CA, United States  
93923  
Balint, Joseph P., 169 Crooks Ave., Clifton, NJ, United States  
07011  
Langone, John J., 7735 Candlegreen, Houston, TX, United States  
77071  
PI US 4699783 871013  
AI US 83-542239 831014 (6)  
RLI Continuation-in-part of Ser. No. US 83-472362, filed on 11 Mar  
1983, now abandoned which is a continuation-in-part of Ser. No. US  
82-366436, filed on 7 Apr 1982, now abandoned  
DT Utility  
EXNAM Primary Examiner: Hazel, Blondel  
LREP Fulbright & Jaworski  
CLMN Number of Claims: 8  
ECL Exemplary Claim: 1  
DRWN 7 Drawing Figure(s); 6 Drawing Page(s)  
LN.CNT 2130

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compositions for the treatment of cancer, such as  
lymphomas and solid tumors, methods of producing these  
compositions, and methods and regimens in using these compositions  
in the treatment of hosts having cancer. The compositions are (1)  
tumor immune preparations which can be prepared by acidification  
or alkalization of an enriched immunoglobulin effluent from  
forced flow electrophoresis of plasma from a normal or a tumor  
bearing host, (2) tumor immune globulin which can be prepared by  
acidifying a Cohn gamma globulin fraction from a normal or a tumor  
bearing host, (3) protein A-IgG preparations which can be prepared  
by perfusion of plasma over protein A from staphylococcus aureus  
Cowans I and precipitating the complex or by incubating protein A  
and purified IgG or IgG in plasma, (4) tumor immune plasma  
preparations which may be prepared by acidification of plasma from  
normal or tumor bearing hosts, and (5) zymosan activated plasma  
which can be prepared by incubating plasma with zymosan and then  
removing the zymosan. Infusing of the compositions alone or in  
combination with each other and with various chemotherapeutic  
agents has resulted in tumoricidal reactions, objective anti-tumor  
effects, and sustained tumor regressions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/085.000  
INCLS: 424/101.000; 530/387.000  
NCL NCLM: 424/178.100  
NCLS: 530/389.700; 530/413.000; 530/419.000; 530/421.000

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Searcher : Shears 308-4994

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGLAUNCH, DRUGB, CANCERLIT' ENTERED AT 16:41:41 ON 07 DEC 1998)

L25 3046 SEA ABB=ON PLU=ON L13  
 L26 760 SEA ABB=ON PLU=ON L25 AND (BR96 OR (BR OR CHIBR OR HBR) (W) 96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR HB(W) (10460 OR 10036) OR MOAB OR MAB OR MONOCLON? OR HYBRIDOMA)  
 L27 7 SEA ABB=ON PLU=ON L26 AND (LE OR LEY OR LEX)  
 L28 204 SEA ABB=ON PLU=ON L26 AND ADMIN?  
 L29 50 SEA ABB=ON PLU=ON L28 AND (IMMUNOTHERAP? OR IMMUN? THERAP?)  
 L30 57 SEA ABB=ON PLU=ON L27 OR L29  
 L31 28 DUP REM L30 (29 DUPLICATES REMOVED)

L31 ANSWER 1 OF 28 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD  
 AN 98-05259 BIOTECHDS

TI **Inhibiting immunoglobulin-induced toxicity resulting from immunotherapy;**  
 using humanized antibody or chimeric antibody produced by antibody engineering

AU Rosok M J; Yelton D E  
 PA Bristol-Squibb  
 LO New York, NY, USA.  
 PI WO 9805787 12 Feb 1998  
 AI WO 97-US13562 1 Aug 1997  
 PRAI US 96-23033 2 Aug 1996

DT Patent  
 LA English

OS WPI: 98-145622 [13]

AN 98-05259 BIOTECHDS

AB A new method for **inhibiting immunoglobulin -induced toxicity** resulting from **Ig immunotherapy** involves: **administering** to a subject an Ig molecule having a variable and a constant regions, where the Ig is modified prior to **administration** by structurally altering multiple **toxicity** associated domains in the constant region so that **Ig-induced toxicity is inhibited;**  
 preventing **Ig-induced toxicity** resulting from **Ig immunotherapy** in a subject, by selecting an **Ig** or **Ig** fusion protein which recognizes and binds to a target which is associated with the disease, structurally altering multiple **toxicity** associated domains in the CH2 domain of the constant region of the Ig, and **administering** the structurally altered Ig or Ig fusion protein under conditions so that the structurally altered Ig fusion protein recognizes and binds the target, alleviating symptoms associated with the disease,

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where the structural alteration of the CH2 domain of the constant region prevents Ig-induced toxicity in a subject; and BR96 antibodies (humanized or chimeric). Nucleic acid encoding the antibody, a plasmid, a host/vector system and a pharmaceutical composition are also claimed. (135pp)

L31 ANSWER 2 OF 28 MEDLINE DUPLICATE 2  
 AN 1998268584 MEDLINE  
 DN 98268584  
 TI Antibody responses in melanoma patients immunized with an anti-idiotypic antibody mimicking disialoganglioside GD2.  
 AU Foon K A; Sen G; Hutchins L; Kashala O L; Baral R; Banerjee M; Chakraborty M; Garrison J; Reisfeld R A; Bhattacharya-Chatterjee M  
 CS Department of Internal Medicine, Lucille Parker Markey Cancer Center, University of Kentucky Medical Center, Lexington 40536-0093, USA.  
 NC R01CA-72018-02 (NCI)  
 SO Clin Cancer Res, (1998 May) 4 (5) 1117-24.  
 Journal code: C2H. ISSN: 1078-0432.  
 CY United States  
 DT (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199809  
 EW 19980903  
 AB We initiated a clinical trial for patients with advanced malignant melanoma treated with an anti-idiotypic antibody that mimics the disialoganglioside GD2. We report the clinical and immune responses of the first 12 patients entered into this trial. Patients received 1-, 2-, 4-, or 8-mg doses of the anti-idiotypic antibody mixed with 100 microg of QS-21 adjuvant every other week, four times, and then monthly. Twelve patients have been on trial for 2-23 months, and all of them have generated immune responses. Patients were removed from the study if they demonstrated disease progression. Hyperimmune sera from all 12 patients revealed an anti-anti-idiotypic Ab3 response, as demonstrated by the inhibition of Ab2 binding to Ab1 by patients' immune sera. To further test the anti-anti-idiotypic response, patients' Ab3 antibodies were affinity purified on Sepharose 4B columns containing adsorbed immunizing anti-idiotypic immunoglobulin. Purified Ab3 of all patients studied inhibited binding of Ab1 to a GD2-positive cell line. Purified Ab3 also inhibited binding of Ab1 to purified GD2, in a manner comparable to equal quantities of purified Ab1. The patient Ab3 was truly an Ab1' because it specifically bound to purified disialoganglioside GD2. The isotypic specificity of the Ab3 antibody was predominantly IgG, with only minimal IgM. The predominant IgG subclass was IgG1, with approximately equal quantities of IgG2, IgG3, and IgG4. These Ab3  
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antibodies reacted specifically with tumor cells expressing GD2 by immune flow cytometry and immunoperoxidase assays. Five patients' Ab3 antibodies studied for antibody-dependent cellular cytotoxicity were positive. One patient had a complete clinical response, with resolution of soft tissue disease, and six patients had stable disease, ranging from 9 to 23 months, and are being continued on vaccine therapy. **Toxicity** consisted of local reaction at the site of the injection, including induration and pain that generally resolved within a few days. Mild fever and chills were observed in 75% of the patients but rarely required acetaminophen. There was no additional **toxicity**, including abdominal pain that was previously seen with infusion of murine **monoclonal** anti-GD2 antibody. Current trials include patients with stage III melanoma and small cell lung cancer. Future trials will attempt to enhance the antitumor response by the addition of interleukin 2, granulocyte macrophage colony-stimulating factor, and other cytokines, together with the 1A7 vaccine.

L31 ANSWER 3 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 1998004762 EMBASE  
 TI Therapy for colon carcinoma xenografts with bispecific antibody-targeted, iodine-131-labeled bivalent hapten.  
 AU Gautherot E.; Bouhou J.; Le Doussal J.-M.; Manetti C.; Martin M.; Rouvier E.; Barbet J.  
 CS E. Gautherot, Imaging and Therapeutics Department, IMMUNOTECH SA, 130 Avenue de Lattre de Tassigny, 13276 Marseille Cedex 9, France  
 SO Cancer, (1997) 80/12 SUPPL. (2618-2623).  
 Refs: 18  
 ISSN: 0008-543X CODEN: CANCAR  
 CY United States  
 DT Journal; Conference Article  
 FS 016 Cancer  
 023 Nuclear Medicine  
 026 Immunology, Serology and Transplantation  
 037 Drug Literature Index  
 048 Gastroenterology  
 LA English  
 SL English  
 AB BACKGROUND. One of the main limitations of radioimmunotherapy (RIT) is the secondary **toxicity** related to the poor therapeutic indices achieved with labeled whole **immunoglobulin** (Ig)G or F(ab')<sub>2</sub> fragments. To overcome this problem, we have developed a two-step targeting method, which we refer to as the Affinity Enhancement System (AES), using a radiolabeled bivalent hapten and a bispecific antibody recognizing the hapten and a target cell antigen. This method has been applied successfully to immunoscintigraphy in carcinoembryonic antigen (CEA)-expressing carcinoma patients and increased tumor to normal tissue uptake ratios have been achieved. The aim of the current study was to  
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evaluate the application of AES to RIT of CEA- expressing solid tumors in an animal model. METHODS. Nude mice grafted with LS174T human colorectal carcinoma were treated either with 111 megabecquerels (MBq) of iodine-131 labeled bivalent diethylenetriamine pentaacetic acid (DTPA) hapten 20 hours after pretargeting by antiCEA x anti-DTPA-indium bispecific antibody or 12 MBq of iodine-131 labeled anti- CEA IgG. RESULTS. Treatment with the IgG induced only a growth delay of 53  $\pm$  5 days but all tumors progressed. Treatment with the AES was highly efficient because tumor growth inhibition was achieved over 150 days. Hematologic and overall toxicity of both treatments were equivalent. CONCLUSIONS. The long term tumor regression consecutive to AES RIT represents a very significant improvement over the use of directly labeled IgG. Toxicity consecutive to AES or IgG RIT were similar despite an administered activity nearly ten times higher with the AES. However, given the efficacy of the AES treatment, a lower dose may afford lower toxicity and significant antitumor effect.

L31 ANSWER 4 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS

AN 98:80489 BIOSIS

DN 01080489

TI Clinical experience with CD64-directed immunotherapy. An overview.

AU Curnow R T

CS Medarex Inc., Annadale, NJ 08801, USA

SO Cancer Immunology Immunotherapy 45 (3-4). 1997. 210-215. ISSN: 0340-7004

LA English

AB The class I IgG receptor (Fc-gamma-RI or CD64 receptor), which is present on key cytotoxic effector cells, has been shown to initiate the destruction of tumor cells in vitro and has been hypothesized to play a role in the destruction of antibody-coated cells such as platelets in idiopathic thrombocytopenia purpura (ITP). This overview summarizes the clinical experience with CD64-directed immunotherapy in cancer patients with the bispecific antibodies MDX-447 (humanized Fab anti-CD64 times humanized Fab anti-(epidermal growth factor receptor, EGFR)) and MDX-H210 (humanized Fab anti-DC64 times Fab anti-HER2/neu), and with the anti-CD64 monoclonal antibody (mAB) MDX-33 (H22) in the modulation of monocyte CD64 in vivo. In an ongoing phase I/II open-label trial with progressive dose escalation (1-15 mg/m<sup>2</sup>), patients with treatment refractory EGFR-positive cancers (renal cell carcinoma (RCC), head and neck, bladder, ovarian, prostate cancer and skin cancer) are treated weekly with intravenous MDX-447, with and without granulocyte-colony-stimulating factor (G-CSF). MDX-447 has been found to be immunologically active at all doses, binding to circulating monocytes and neutrophils (when given with G-CSF),

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causing monocytopenia and stimulating increases in circulating plasma cytokines. MDX-447 is well tolerated, the primary toxicities being fever, chills, blood pressure lability, and pain/myalgias. Of 36 patients evaluable for response, 9 have experienced stable disease of 3-6 month's duration. The optimal dose and the maximal tolerated dose (MTD) have yet to be defined; dose escalation continues to define better the dose, toxicity, and the potential therapeutic role of this bispecific antibody. Three MDX-H210 phase II trials are currently in progress, all using the intravenous dose of 15 mg/m<sup>2</sup> given with granulocyte/macrophage (GM-CSF). These consist of one trial each in the treatment of RCC patients, patients with prostrate cancer, and colorectal cancer patients, all of whom have failed standard therapy. At the time of writing, 11 patients have been treated in these phase II trials. Four patients have demonstrated antitumor effects. Patients demonstrating responses include 2 with RCC and 2 with prostate cancer. One RCC patient has had a 54% reduction in size of a hepatic metastatic lesion and the other has had a 49% decrease in the size of a lung metastasis with simultaneous clearing of other non-measurable lung lesions. Regarding the two patients with prostate cancer, one has had a 90% reduction in serum prostate-specific antigen (PSA; 118-11 ng/ml), which has persisted for several months; the other patient with prostate has had a 70% reduction of serum PSA (872 ng/ml to 208 ng/ml) within the first month of treatment. Both patients have also demonstrated symptomatic improvement. In a completed phase I and in ongoing phase I/II clinical trials, patients with treatment-refractory HER2/neu positive cancers (breast, ovarian, colorectal, prostate) have been treated with MDX-H210, which has been given alone and in conjunction with G-CSF, GM-CSF, and interferon gamma (IFN-gamma). These trials have been open-label, progressive dose-escalation (0.35-135 mg/m<sup>2</sup>) studies in which single, and more often, multiple weekly doses have been administered. MDX-H210 has been well tolerated, with untoward effects being primarily mild-to-moderate flu-like symptoms. The MTD has not yet been defined. MDX-H210 is immunologically active, binding to circulating monocytes, causing monocytopenia, as well as stimulating increases in plasma cytokine levels. Furthermore, some patients have evidence of active antitumor immunity following treatment with MDX-210. Antitumor effects have been seen in response to MDX-H210 administration; these include 1 partial, 2 minor, and 1 mixed tumor response; 15 protocol-defined stable disease responses have occurred. In a completed phase I trial, MDX-33 was administered as a single intravenous dose to 17 normal subjects in order to assess its potential as an immunomodulator for the treatment of idiopathic thrombocytopenia purpura and other immune disorders. Doses of 1.5, 3.0, 5.0, and 7.5 mg/m<sup>2</sup> were administered. The variables evaluated in response to MDX-33 were circulating monocyte and neutrophil counts, monocyte CD64-mediated phagocytosis, monocyte CD64 modulation, MDX-33 pharmacokinetics, and various safety parameters. MDX-33 is well

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tolerated at doses of 5.0 mg/m<sup>2</sup> or less, the primary toxicities being chills, low-grade fever, headache, and muscle aches. Persistent binding of MDX-33 to 80-99% of circulating monocytes is seen for at least 6 days; down-modulation of monocyte CD64 occurs and also lasts more than 6 days. Monocyte CD64-mediated phagocytosis is significantly inhibited at all doses of MDX-33. At the 3.0 mg/m<sup>2</sup> and 5.0 mg/m<sup>2</sup> dose, phagocytosis is fully inhibited for at least 6 days, returning to baseline levels by 20 days after dosing. These results clearly demonstrate that immunomodulation of monocyte CD64 by the mAb MDX-33 can be accomplished with minimal clinical toxicity, and further indicate the potential of MDX-33 in the treatment of ITP and other auto-immune disorders. In conclusion, the results from completed and ongoing clinical trials with the CD64-directed bsAB MDX-447 and MDX-H210 demonstrate excellent tolerability in association with promising antitumor effects in tumors that have become refractory to all available therapies. Also promising are the results from the trial of the CD64-directed mAb, MDX-33, which show the ability to modulate monocyte CD64 in the clinical setting. Studies are currently being conducted to elucidate the full potential of these and other approaches using CD64-directed immunotherapy

L31 ANSWER 5 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 97158034 EMBASE  
 TI Recent clinical trials in the rheumatic diseases.  
 AU Matteson E.L.  
 CS Dr. E.L. Matteson, Division of Rheumatology, Department of Internal Medicine, Mayo Clinic Graduate School Medicine, Rochester, MN 55905, United States  
 SO Current Opinion in Rheumatology, (1997) 9/2 (95-101).  
 Refs: 49  
 ISSN: 1040-8711 CODEN: CORHES  
 CY United States  
 DT Journal  
 FS 031 Arthritis and Rheumatism  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LA English  
 SL English  
 AB This paper reviews clinical trials that have been published during the course of the past year on the rheumatologic diseases. The greatest number of clinical trials were done in rheumatoid arthritis. These trials show promising results for combination therapy with disease-modifying antirheumatic drugs, whereas results of studies with monoclonal antilymphocyte antibodies have been disappointing. The role of oral collagen remains to be defined. Nonsteroidal anti-inflammatory drugs with selective cyclooxygenase-2 (Cox-2) inhibition may have a more favorable

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toxicity profile and are likely to find wide use. As adjuvant therapy, trimethoprim-sulfamethoxazole appears to be useful in preventing relapses in Wegener's granulomatosis, and patients develop fewer infections. With the exception of juvenile rheumatoid arthritis, intravenous immunoglobulin therapy appeared ineffective in the diseases studied. The inclusion of more standardized and disease-specific outcome measures has enhanced the quality of clinical trials in rheumatology and their applicability to rheumatologic practice.

L31 ANSWER 6 OF 28 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD  
 AN 97-38897 DRUGU P  
 TI Maximising the therapeutic window of the anti-carcinoma single-chain immunotoxin BR96 sFv-PE40.  
 AU Siegall C B; Chace D; Mixan B; Sugai J; Linsley P S; Haggerty H; Warner G; Davidson T  
 CS Bristol-Squibb  
 LO Seattle, Wash.; Syracuse, N.Y., USA  
 SO Proc.Am.Assoc.Cancer Res. (38, 88 Meet., 28, 1997) ISSN: 0197-016X  
 AV Bristol-Myers Squibb, Pharmaceutical Research Inst., Seattle, WA 98121, U.S.A.  
 LA English  
 DT Journal  
 FA AB; LA; CT  
 FS Literature  
 AN 97-38897 DRUGU P  
 AB Immunogenicity and vascular leak syndrome are the most limiting toxicities of the single-chain immunotoxin BR96 sFv-PE40, which binds to the **Ley** antigen. BR96 sFv-PE40 is a potent antitumor agent that has been shown to cure established human carcinoma xenografts implanted in mice and rats, and is currently being evaluated in a phase I clinical trial. Administration of BR96 sFv-PE40 with either deoxyspergualin, dexamethasone or CTLA-4 Ig, caused a reduction of antiimmunotoxin Ab's which were able to induce rapid clearance of the immunotoxin and potential kidney toxicities. Prophylactic administration of antiinflammatory agents including NSAIDs, dexamethasone, and PLA2 inhibitors, was found to inhibit BR96 sFv-PE40 induced VLS. (conference abstract).  
 ABEX BR96 sFv-PE40 was immunogenic in mice, rats, and dogs by approximately 10 days post-administration. Concomitant administration of BR96 sFv-PE40 and the immunosuppressive agents deoxyspergualin, dexamethasone, or CTLA4-Ig resulted in a reduction of antiimmunotoxin Ab's which were able to induce rapid clearance of the immunotoxin and potential kidney toxicities. Using rats, in which high-dose BR96 sFv-PE40 induces VLS and pulmonary edema, prophylactic

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administration of antiinflammatory agents including NSAIDs, dexamethasone, and PLA2 inhibitors, was found to inhibit VLS. Combination therapy of BR96 sFv-PE40 and the chemotherapeutic agent paclitaxel were found to induce greater antitumor effects in rodents carrying large tumor burdens than either agent alone, and without increasing overall toxicity. (RPG)

L31 ANSWER 7 OF 28 MEDLINE DUPLICATE 3  
 AN 96420258 MEDLINE  
 DN 96420258  
 TI Anti-graft-versus-host disease effect of DT390-anti-CD3sFv, a single-chain Fv fusion immunotoxin specifically targeting the CD3 epsilon moiety of the T-cell receptor.  
 AU Vallera D A; Panoskaltsis-Mortari A; Jost C; Ramakrishnan S; Eide C R; Kreitman R J; Nicholls P J; Pennell C; Blazar B R  
 CS Department of Therapeutic Radiology, University of Minnesota Hospital and Clinics, Minneapolis 55455, USA.  
 NC PO1-CA21737 (NCI)  
 RO1-AI34495 (NIAID)  
 RO1-CA36725 (NCI)  
 +  
 SO BLOOD, (1996 Sep 15) 88 (6) 2342-53.  
 Journal code: A8G. ISSN: 0006-4971.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
 EM 199612  
 AB In a recent study, we showed that an immunotoxin (IT) made with a conventional monoclonal antibody targeting the CD3 epsilon moiety of the T-cell receptor (TCR) had a potent, but partial, graft-versus-host disease (GVHD) effect (Vallera et al, Blood 86:4367, 1995). Therefore, in this current study, we determined whether a fusion immunotoxin made with anti-CD3 single-chain Fv (sFv), the smallest unit of antibody recognizing antigen, would have anti-GVHD activity. A fusion protein was synthesized from a construct made by splicing sFv cDNA from the hybridoma 145-2C11 to a truncated form of the diphtheria toxin (DT390) gene. DT390 encodes a molecule that retains full enzymatic activity, but excludes the native DT binding domain. The DT390-anti-CD3sFv hybrid gene was cloned into a vector under the control of an inducible promoter. The protein was expressed in Escherichia coli and then purified from inclusion bodies. The DT390 moiety of the protein had full enzymatic activity compared with native DT and DT390-anti-CD3sFv, with an IC50 of 1 to 2 nmol/L against phytohemagglutinin-stimulated and alloantigen-stimulated T cells. Specificity was shown (1) by blocking the IT with parental anti-CD3 antibody, but not with a control antibody; (2) by failure of  
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DT390-anti-CD3sFv to inhibit lipopolysaccharide-stimulated murine B cells; (3) by failure of an Ig control fusion protein, DT390-Fc, to inhibit T-cell responses; and (4) with in vivo immunohistochemistry studies. GVHD was studied in a model in which C57BL/6 (H-2b)-purified lymph node T cells were administered to major histocompatibility complex (MHC) antigen disparate unirradiated C.B.-17 scid (H-2d) mice to assess GVHD effects in the absence of irradiation toxicity. Flow cytometry studies showed that donor T cells were expanded 57-fold and histopathologic analysis showed the hallmarks of a lethal model of GVHD. Control mice receiving phosphate-buffered saline showed 17% survival on day 80 after bone marrow transplantation, and mice receiving 2 micrograms DT390-Fc fusion toxin control administered in 2 daily doses for 6 days (days 0 through 5) had a 43% survival rate. In contrast, 86% of mice receiving the same dose of DT390-anti-CD3sFv were survivors on day 80, a significant improvement, although survivors still showed histopathologic signs of GVHD. These findings suggest that new anti-GVHD agents can be genetically engineered and warrant further investigation of fusion proteins for GVHD treatment.

L31 ANSWER 8 OF 28 MEDLINE  
 AN 96191015 MEDLINE  
 DN 96191015  
 TI Short course single agent therapy with an LFA-3-IgG1 fusion protein prolongs primate cardiac allograft survival.  
 AU Kaplon R J; Hochman P S; Michler R E; Kwiatkowski P A; Edwards N M; Berger C L; Xu H; Meier W; Wallner B P; Chisholm P; Marboe C C  
 CS Department of Surgery, College of Physicians and Surgeons, Columbia University, New York, New York 10032, USA.  
 SO TRANSPLANTATION, (1996 Feb 15) 61 (3) 356-63.  
 Journal code: WEJ. ISSN: 0041-1337.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 EM 199608  
 AB The interaction of T cell costimulatory molecules with their ligands is required for optimal T cell activation. Interference with such interactions can induce antigen unresponsiveness and delay xeno- and allograft rejection. We have previously shown that LFA3TIP, a soluble human lymphocyte function-associated antigen (LFA)-3 construct, binds CD2 and inhibits responses of human T cells in vitro. This study reports the first use of a human fusion protein, LFA3TIP, to significantly prolong primate cardiac allograft survival. Based on our observations that LFA3TIP inhibits baboon allogeneic mixed lymphocyte reactions, we gave baboon recipients of heterotopic cardiac allografts injections of LFA3TIP, 3 mg/kg i.v., for 12 consecutive days, starting 2 days before

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transplantation. This regimen delayed graft rejection from an average of 10.6 +/- 2.3 days for human IgG-treated controls (n = 5) to an average of 18.0 +/- 5.3 days for LFA3TIP-injected animals (n = 7; P < or = 0.01). Grafts from LFA3TIP-treated animals showed markedly diminished coronary endothelialitis as compared with control animals. LFA3TIP reached peak serum levels of approximately 100 micrograms/ml after 7-9 injections and persisted in the 10-micrograms/ml range for 1 to 2 weeks after the final injection. Despite these blood levels, circulating antibodies to LFA3TIP were not detected in the serum. No renal or hepatic toxicity was noted. The possible mechanism by which LFA3TIP acts to inhibit graft rejection is discussed; success in prolonging graft survival when LFA3TIP is used as a single-agent therapy suggests great potential for this novel therapeutic agent.

L31 ANSWER 9 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 95259508 EMBASE  
 TI Inhibition of lymphoma growth in vivo by combined treatment with hydroxyethyl starch deferoxamine conjugate and IgG monoclonal antibodies against the transferrin receptor.  
 AU Kemp J.D.; Cardillo T.; Stewart B.C.; Kehrberg E.; Weiner G.; Hedlund B.; Naumann P.W.  
 CS 5238 Carver, University of Iowa Hospitals, Iowa City, IA 52242, United States  
 SO Cancer Research, (1995) 55/17 (3817-3824).  
 ISSN: 0008-5472 CODEN: CNREA8  
 CY United States  
 DT Journal  
 FS 016 Cancer  
 025 Hematology  
 037 Drug Literature Index  
 LA English  
 SL English  
 AB Synergistic inhibition of hematopoietic tumor growth can be observed in vitro when the iron chelator deferoxamine (DFO) is used in combination with an IgG mAb against the anti-transferrin receptor antibody (ATRA). Our goal was to ascertain whether similar findings could be seen in vivo. A high molecular weight conjugate of deferoxamine, known as hydroxyethyl starch (HES) DFO or HES-DFO, was tested in conjunction with C2, a well-defined rat antimouse transferrin receptor mAb, against the 38C13 tumor in C3H/HeN mice. It was shown that while neither HES-DFO alone nor C2 alone produced consistent, significant inhibition of tumor growth, the combination of HES- DFO and C2 produced virtually complete inhibition of initial tumor outgrowth. The latter combination failed, however, to inhibit the growth of established tumors. It was then found that when C2 was used in conjunction with RL34, another IgG ATRA, the two

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ATRAS were themselves capable of causing synergistic inhibition of the growth of 38C13 in vitro. When the two IgG ATRAS were used together in vivo, regressions of established tumors were observed. Moreover, the addition of HES-DFO to the IgG ATRA pair then caused more frequent regressions. Although there was never any obvious toxicity seen with a single IgG ATRA, the use of the IgG ATRA pair was associated with sporadic mortality. In addition, although HES-DFO by itself was also not associated with any obvious toxicity, combined treatment with HES-DFO and a single ATRA resulted in death due to bacterial infection in about half of the mice after 10-15 days. Combined treatment with HES-DFO and the ATRA pair resulted in death attributed to infection in nearly all of the mice after 6 days. Thus, an iron deprivation treatment protocol with HES-DFO and IgG ATRAS produced both a significant antitumor effect and an increased risk of infection in a taurine model system.

L31 ANSWER 10 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE  
5  
AN 95346573 EMBASE  
TI In vivo cytotoxicity of **monoclonal** antibody-carboplatin immunoconjugates and tissue platinum distribution in tumor-bearing nude mice.  
AU Takeda A.; Miyoshi T.; Isono K.  
CS Department of Surgery, Yokohama Rosai Hospital, 3231 Kozukue-cho, Kohoku-ku, Yokohama 222, Japan  
SO Biotherapy, (1995) 9/10 (1253-1257).  
ISSN: 0914-2223 CODEN: BITPE  
CY Japan  
DT Journal  
FS 016 Cancer  
026 Immunology, Serology and Transplantation  
037 Drug Literature Index  
LA Japanese  
SL English; Japanese  
AB In vivo anti-tumor effect of **monoclonal** antibody (1B2) carboplatin conjugates (immunoconjugates) and tissue platinum distribution were evaluated in nude mice bearing human ovarian cancer. Animals given immunoconjugates showed significantly stronger tumor growth suppression than those given the same dose drug alone, antibodies alone, or nonspecific mouse IgG drug conjugates. Thirty minutes later, after **administration**, platinum accumulation in the tumor was significantly higher in the CBDCA-conjugates group than in the other group. Almost similar results were obtained two or twenty four hours later. But serum platinum concentrations of a lower level were observed in every experimental group. We conclude that **immunotargeting therapy** guided CBDCA-conjugates reduced the systemic

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**toxicity** of the drug and induced an earlier **inhibition** of tumor growth.

L31 ANSWER 11 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 96019838 EMBASE  
 TI Therapy and imaging of pancreatic carcinoma xenografts with radioiodine-labeled chimeric **monoclonal** antibody A10 and its Fab fragment.  
 AU Kamigaki T.; Yamamoto M.; Ohyanagi H.; Ohya M.; Shimazoe T.; Kono A.; Ohtani W.; Narita Y.; Ohkubo M.; Saitoh Y.  
 CS First Department of Surgery, Kobe University School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650, Japan  
 SO Japanese Journal of Cancer Research, (1995) 86/12 (1216-1223). ISSN: 0910-5050 CODEN: JJCREP  
 CY Japan  
 DT Journal  
 FS 016 Cancer  
 023 Nuclear Medicine  
 026 Immunology, Serology and Transplantation  
 048 Gastroenterology  
 037 Drug Literature Index  
 LA English  
 SL English  
 AB Recombinant mouse/human chimeric **monoclonal** antibody A10 (ch-A10) and its Fab fragment (ch-Fab) react with carcinoembryonic antigen on various gastrointestinal carcinomas. We performed biodistribution studies with 125I-labeled ch-A10 and ch-Fab in an antigen-positive human pancreatic carcinoma (BxPC-3) xenograft model. We also evaluated the anti-tumor effect of 131I-labeled ch-A10 and studied the detection of BxPC-3 xenografts with 123I-labeled ch-Fab in whole body scintigraphy. In comparative biodistribution studies, the tumor uptake of 125I-labeled ch-A10 was significantly greater than that of 125I-labeled ch-Fab 24 h post-injection. However, the tumor-to-blood ratio was 46.8 for ch-Fab at 24 h post-injection, while it was only 1.4 for ch-A10. Microautoradiography studies showed that ch-Fab penetrated more uniformly into the tumor nodules than did ch-A10. In mice given a therapeutic dose of 131I-labeled ch-A10, a significant **inhibition** of tumor growth was seen, while control 131I-labeled human IgG did not affect tumor growth. Leukocyte **toxicity** was observed within 3 weeks after injection of 131I-labeled ch-A10, but leukocyte counts recovered to normal levels at 8 weeks post-injection. In whole-body scintigraphy, clear and rapid tumor imaging was obtained with 200 .mu.Ci of 123I-labeled ch-Fab 24 h post-injection. These results suggest that radioiodine-labeled chimeric A10 antibodies could potentially be useful candidates for radioimmunotherapy and radioimmunodetection of pancreatic carcinomas.

L31 ANSWER 12 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 94244558 EMBASE  
 TI Mechanisms of endothelial cell injury in vasculitis.  
 AU Pall A.A.; Savage C.O.S.  
 CS Medical School, Department of Medicine, University of Birmingham,  
 Edgbaston, Birmingham B15 2TT, United Kingdom  
 SO SPRINGER SEMIN. IMMUNOPATHOL., (1994) 16/1 (23-37).  
 ISSN: 0344-4325 CODEN: SSIMDV  
 CY Germany, Federal Republic of  
 DT Journal  
 FS 005 General Pathology and Pathological Anatomy  
 025 Hematology  
 026 Immunology, Serology and Transplantation  
 031 Arthritis and Rheumatism  
 037 Drug Literature Index  
 LA English  
 SL English  
 AB The aetiology of the primary systemic vasculitides remains obscure. Recent years have seen significant advances in our understanding of inflammation and in particular the role of and interaction between the vascular endothelium, mediators and immune effector cells. This has helped to further elucidate those specific processes relevant to vasculitis which result in endothelial cell damage. In Wegener's granulomatosis and microscopic polyarteritis the evidence favours an autoimmune inflammatory response characterised by specific mediators in which the endothelium is both target and active participant current treatment of these disorders with combinations of corticosteroids and cytotoxics is highly effective in inducing remission. However, long-term use of this therapy is potentially **toxic** and there remains also a significant risk of relapse. It is hoped that increased understanding of the pathogenesis of systemic vasculitis will enable more specific, less **toxic** and more effective therapies to be defined. Jayne et al. have suggested a beneficial effect of intravenous pooled normal human **immunoglobulin** (IVIG) in patients with ANCA-positive vasculitis. In vitro studies have shown that IVIG contains antiidiotypic antibodies to NACA and AECA, capable of **inhibiting** the binding of these autoantibodies to their autoantigens. In vivo, IVIG may also provide the immunoregulatory elements needed for the idotype network and control of the autoimmune repertoire. Mathieson et al. successfully used **monoclonal** antibodies to T cells (Campath-H directed against CDw52) in a patient with ANCA-negative dermal lymphocytic vasculitis. **Monoclonal** antibodies to CAMs have been used in human renal transplant rejection and reduced the inflammation and proteinuria in animal models of anti-glomerular basement membrane disease. In vasculitis, the therapeutic use of specific anti-CAM antibodies may result from further definition of the role of CAMs. Increased understanding of the pathogenesis of systemic vasculitis

Searcher : Shears 308-4994

is likely to provide the basis for the use of more specific immunotherapies in the future.

L31 ANSWER 13 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 94146767 EMBASE  
 TI New developments in the treatment of systemic vasculitis.  
 AU Gross W.L.  
 CS DIMCI, Rheumaklinik Bad Bramstedt, 24572 Bad Bramstedt, Germany,  
 Federal Republic of  
 SO CURR. OPIN. RHEUMATOL., (1994) 6/1 (11-19).  
 ISSN: 1040-8711 CODEN: CORHES  
 CY United States  
 DT Journal  
 FS 006 Internal Medicine  
 026 Immunology, Serology and Transplantation  
 031 Arthritis and Rheumatism  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LA English  
 SL English  
 AB Although precise diagnosis of the systemic vasculitides can provide general prognostic information and help to guide initial therapy, recent studies on the long-term clinical course have revealed considerable variation in clinical severity. Therefore, anatomic distribution of involvement and speed of progression should be the principle determinants of the intensity of immunosuppressive therapy. In progressive pulmonary or renal disease, eg, Wegener's granulomatosis, aggressive 'standard' therapy is obligatory, eg, daily cyclophosphamide and glucocorticoids. Such regimens, however, should be applied with caution in chronic or indolent and abortive forms of systemic vasculitis, because follow-up studies (eg, in Wegener's granulomatosis) have revealed treatment-associated morbidity rates of up to 42%, disease-related morbidity, and a high incidence of relapse under treatment. Moreover, less toxic therapeutic strategies are being pursued with remarkable success: low- dose weekly methotrexate, monthly intravenous or oral pulses of cyclophosphamide plus glucocorticoids, and high-dose intravenous immunoglobulin. Long-term remission of intractable (non-antineutrophil cytoplasmic antibody-associated) systemic vasculitis has been achieved using humanized monoclonal antibodies (ie, anti-CD4/anti-CDw52); and amelioration of glomerulonephritis in immune complex diseases (eg, systemic lupus erythematosus) has been achieved with nafamostat mesilate, an inhibitor of complement serine proteases. In addition, leukocytoclastic vasculitis has been effectively controlled with pentoxifylline, presumably by neutralizing proinflammatory cytokines, and hepatitis C virus-associated mixed cryoglobulinemia has been successfully treated with interferon alfa.

L31 ANSWER 14 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 6

AN 93:230647 BIOSIS

DN BA95:121822

TI LE-GAMMA SPECIFIC ANTIBODY WITH POTENT ANTI-TUMOR ACTIVITY  
IS INTERNALIZED AND DEGRADED IN LYSOSOMES.

AU GARRIGUES J; GARRIGUES U; HELLSTOM I; HELLSTROM K E

CS BRISTOL-MYERS SQUIBB COMPANY, 3005 FIRST AVENUE, SEATTLE, WA 98121.

SO AM J PATHOL 142 (2). 1993. 607-622. CODEN: AJPAA4 ISSN: 0002-9440

LA English

AB BR96 is a monoclonal antibody (Mab)

that recognizes many human carcinomas and can kill antigen-positive tumor cells in vitro. Using both gold and radiolabeled Mab, the distribution and cellular processing of BR96 during cytolysis has been determined. After a brief (< 3 minutes) Mab treatment, cells in suspension are stained by the nuclear viability dye propidium iodide. Whole Mab and F(ab')<sub>2</sub> fragments are equally cytotoxic; monovalent F(ab) fragments, however, have no effect on dye uptake unless cross-linked with goat anti-mouse IgG. The level of toxicity is dependent on both Mab dose and on cell surface receptor density. Cell contact may regulate receptor expression. BR96 receptors are more abundant on cells migrating into the open areas of a scratch wounded confluent culture than on the adjacent contact-inhibited cells. BR96 can also inhibit

the anchorage-independent growth of tumor cells in soft agar showing that its effects on propidium iodide staining are not due to transient changes in membrane permeability. Immunogold electron microscopy reveals that, after a 1-minute treatment, BR96 induces significant infolding of the plasma membrane and that internalized Mab is localized to these structures. Immediately thereafter, large cell surface and intracellular vesicles form, mitochondria are swollen, and membrane integrity is lost. Therefore, BR96 seems to cause morphological changes characteristic of necrosis rather than apoptosis. When bound to adherent carcinoma cells, BR96 is distributed uniformly on the apical surface of cells labeled at 4 C and is enriched at points of cell substratum contact. Upon warming of the cells to 37 C, BR96 localizes in small perinuclear clusters and the cell margin is now devoid of label. Immunogold electron microscopy reveals that BR96 undergoes receptor mediated internalization and is localized within the same coated pits, endosomes, and lysosomes as the transferrin receptor. Quantitative studies using iodinated BR96 show that after 6 hours of chase, a maximum of 53% of the radiolabel is located within the intracellular pool. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis indicates that 84% of this fraction is nondegraded. BR96 probably cycles between the medium and intracellular pools because the remainder of the radiolabel is in the medium as intact Mab. By 24 hours of chase, the intracellular fraction drops to 30%, while

Searcher : Shears 308-4994



the remaining 70% is present in the culture medium, mostly as low molecular weight degradation products.

L31 ANSWER 15 OF 28 PROMT COPYRIGHT 1998 IAC

AN 93:557033 PROMT

TI Phase I Trial of Anti-Idiotypic Antibody Vaccine Melimmune-2 TM in Patients with Resected Poor Risk Malignant Melanoma

SO Cancer Weekly, (22 Mar 1993) pp. N/A.

LA English

WC 358

\*FULL TEXT IS AVAILABLE IN THE ALL FORMAT\*

AB AUTHORS: J.L. Murray, R.W. Carlson, K.M. Adler, H. Brewer, L. Bendon, S. Raychaudhuri and J. Merritt. University of Texas M.D. Anderson Cancer Center, Houston, Texas; Stanford University, Stanford, California, and IDEC Pharmaceuticals, LaJolla, California. According to an abstract presented by the authors to the Specific Immunotherapy of Cancer Vaccines Conference, held January 21-24, 1993, in Washington, D.C., "The anti -idiotypic Murine monoclonal antibody Melimmune-2( TM) (Ab(2)) is a surrogate antigen for the higher molecular weight proteoglycan (MPG) expressed by >80% of human malignant melanoma. We performed a Phase I trial in 13 melanoma patients with resected AJCC Stage II, III or IV disease to determine toxicity, optimal dosing schedule and immunologic response. Melimmune-2 (2 mg) was mixed with either 100 or 200 ug of novel adjuvant SAF-m and administered as either a single i.m. injection (100 ug SAF-m/inj; 7 pts) or two split injections at separate sites (100 ug SAF-m/inj; 6 pts) every 2 weeks x 4, followed by every 8 weeks x 2 for a total of 6 vaccinations. Sera were collected for measurement of total immune response; Ab(3) was determined by direct binding to Melimmune-2 (HAMA depleted serum) as well as by inhibition RIA. Toxicity was not dependent on SAF-m dose or numbers of injections and consisted of local erythema and induration at the injection site along with fever, headaches and myalgias. Two patients developed moderately severe fever and arthralgias; one of the two had a self-limited episode of low grade asymptomatic anterior uveitis. Both had been PPD(+) prior to study. HAMA to Melimmune-2 antibodies (total response) were measured in all patients; titers ranged from 1:128 to 1:8192. IgG anti-anti-idiotypic antibodies were detected in all patients (range; 1:20 to 1:1000) and increased as a result of repeated immunizations. Affinity-purified Ab(3) bound to MPG in an RIA, and immunoprecipitated the 400 and 25 kD forms of MPG from a melanoma cell line. Four patients have recurred to date; there was no correlation between disease free interval and development of total HAMA or Ab(3) titers. In summary, Melimmune-2 + SAF-m is safe and immunogenic at the above doses and schedule. Single site immunization appears as efficacious as split dosing."

Searcher : Shears 308-4994

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L31 ANSWER 16 OF 28 CANCERLIT  
 AN 92686024 CANCERLIT  
 DN 92686024  
 TI IMMUNOTOXINS.  
 AU Spitler L E  
 CS Northern California Melanoma Center, San Francisco, CA.  
 SO Non-serial, (1991). Principles of Cancer Biotherapy. Second Edition.  
 Oldham RK, ed. New York, Marcel Dekker, p. 433-56, 1991.  
 DT Book; (MONOGRAPH)  
 (REVIEW, ACADEMIC)  
 General Review; (REVIEW)  
 FS ICDB  
 LA English  
 EM 199211  
 AB Immunotoxins consist of a **monoclonal antibody (MAb)**  
 ) or other targeting agent conjugated to a toxin that can kill  
 cells. The term 'immunotoxin' generally has been reserved for  
 conjugates in which the **toxic moiety** is a ribosomal-  
**inhibiting** protein. Such proteins occur naturally in a  
 variety of bacteria, plants and animals. Preclinical studies,  
 clinical trials and issues related to **immunotoxin**  
**therapy** are reviewed. Topics include in vivo and in vitro  
 studies; clinical results (melanoma, breast cancer, colorectal  
 cancer, leukemia/lymphoma, ovarian cancer and graft-vs-host disease  
 [GvHD]); and questions for second-generation studies (stability of  
 conjugates in vivo, cellular heterogeneity, access and localization  
 in tumor, biodistribution, immune response and potentiators).  
 Preclinical and clinical studies have shown clearly the potential of  
 immunotoxins for targeted therapy. Immunotoxins can be  
**administered** safely, and side effects from the ricin A-chain  
 component are transient and well tolerated. Severe **toxicity**  
 can result if the **MAb** has unrecognized cross-reactivity  
 with normal tissues and targets the toxin inappropriately to an  
 unwanted target. There is an immune response to both the murine  
**Ig** and toxin components of immunotoxin, except in some  
 patients with leukemia and lymphoma, which precludes repeated  
 courses of treatment. Encouraging results in lymphomas, leukemias  
 and GvHD suggest that it is possible to achieve efficacy following  
 in vivo **administration** of immunotoxin. Impressive  
 responses have been observed in patients with solid tumors treated  
 with immunotoxins, but the reasons for these responses are not  
 understood. (108 Refs)

L31 ANSWER 17 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.  
 AN 91313489 EMBASE  
 TI Immunotoxins constructed with anti-CD25 **monoclonal**  
 antibodies and deglycosylated ricin A-chain have potent anti-tumour  
 Searcher : Shears 308-4994

effects against human Hodgkin cells in vitro and solid Hodgkin tumours in mice.

AU Engert A.; Martin G.; Amlot P.; Wijdenes J.; Diehl V.; Thorpe P.  
 CS Cancer Immunobiology Center, University of Texas Southwestern, 5323  
 Harry Hines Blvd., Dallas, TX 75235, United States  
 SO INT. J. CANCER, (1991) 49/3 (450-456).  
 ISSN: 0020-7136 CODEN: IJCNW  
 CY United States  
 DT Journal  
 FS 016 Cancer  
 026 Immunology, Serology and Transplantation  
 037 Drug Literature Index  
 LA English  
 AB Twenty-three monoclonal antibodies (MAbs)  
 against the IL-2 receptor .alpha.-chain (CD25) were evaluated as  
 ricin A-chain immunotoxins for the treatment of Hodgkin's disease.  
 Primary screening used an indirect assay in which the cells were  
 treated with the test antibody followed by Fab' immunotoxin against  
 mouse immunoglobulin. This screening identified 5  
 MAbs which inhibited protein synthesis in L540  
 Hodgkin cells by 50% at a concentration (IC50) of  $6 \times 10^{-11}$  M or  
 less: RFT5.gamma.1, RFT5.gamma.2a, B-B10, B-F2 and B-G3. These  
 MAbs were then linked directly to deglycosylated ricin  
 A-chain (dgA) and were confirmed to have potent and specific  
 toxicity for L540 cells. The immunotoxins had the following  
 potency order: RFT5.gamma.1 > RFT5.gamma.2a > B-B10 > B-F2 > B-G3.  
 The most effective immunotoxin, RFT5.gamma.1.cntdot.dgA, had an IC50  
 value of  $7 \times 10^{-12}$  M, which is the same as that of whole ricin. In  
 vivo, a single intravenous injection of 48 .mu.g of  
 RFT5.gamma.1.cntdot.dgA, RFT5.gamma.2a.cntdot.dgA, B-B10.cntdot.dgA  
 or B-F2 induced lasting complete remissions in 78, 66, 50 and 44%,  
 respectively, of nude mice bearing subcutaneous solid L540 tumours  
 of 0.7 cm diameter. Two tumours which regrew after B-B10.cntdot.dgA  
 treatment were re-established in tissue culture. Both had reduced  
 sensitivity to B-B10.cntdot.dgA in vitro but not to immunotoxins  
 recognizing different antigens on Hodgkin cells. The MAbs  
 that produced the most potent immunotoxins, RFT5.gamma.1,  
 RFT5.gamma.2a and B-B10, had no significant cross-reactivity with  
 normal human tissues outside the lymphoid system as judged from  
 indirect immunoperoxidase staining of frozen sections. By contrast,  
 B-F2 strongly stained normal human renal tubules.

L31 ANSWER 18 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 7  
 AN 91:72157 BIOSIS  
 DN BA91:40817  
 TI ACTIVE SPECIFIC IMMUNOTHERAPY IN PATIENTS WITH MELANOMA A  
 CLINICAL TRIAL WITH MOUSE ANTIIDIOTYPIC MONOCLONAL  
 ANTIBODIES ELICITED WITH SYNGENEIC ANTI-HIGH-MOLECULAR-WEIGHT-  
 MELANOMA-ASSOCIATED ANTIGEN MONOCLONAL ANTIBODIES.

Searcher : Shears 308-4994

AU MITTELMAN A; CHEN Z J; KAGESHITA T; YANG H; YAMADA M; BASKIND P;  
 GOLDBERG N; PUCCIO C; AHMED T; ARLIN Z; FERRONE S  
 CS NEW YORK MED. COLL., VALHALLA, NY 10595.  
 SO J CLIN INVEST 86 (6). 1990. 2136-2144. CODEN: JCINAO ISSN: 0021-9738  
 LA English  
 AB In two clinical trials the mouse antiidiotypic **monoclonal**  
 antibody (**MAb**) MF11-30, which bears the internal image of  
 human high-molecular-weight-melanoma-associated antigen (HMW-MAA) was  
**administered** by subcutaneous route without adjuvants to  
 patients with stage IV malignant melanoma on day 0, 7, and 28.  
 Additional injections were **administered** if  
 anti-antiidiotypic antibodies were not found or their titer  
 decreased. In the first phase I trial with 16 patients the initial  
 dose was 0.5 mg per injection and escalated to 4 mg per injection.  
 Neither **toxicity** nor allergic reactions were observed  
 despite the development of anti-mouse Ig antibodies. Minor  
 responses were observed in three patients. In a second clinical trial  
**MAB** MF11-30 was **administered** to 21 patients at a  
 dose of 2 mg per injection, since this dose had been shown in the  
 initial study to be effective in inducing anti-antiidiotypic  
 antibodies. Two patients were inevaluable; in the remaining 19  
 patients, the average duration of treatment was 34 wk. In this trial  
 as well, neither **toxicity** nor allergic reactions were  
 observed. 17 of the 19 immunized patients increased the levels of  
 anti-mouse Ig antibodies and 16 developed antibodies that  
**inhibit** the binding of antiidiotypic **MAB** MF11-30 to  
 the immunizing anti-HMW-MAA **MAB** 225.28. One patient  
 increased the level of anti-HMW-MAA antibodies. One patient achieved  
 a complete remission with disappearance of multiple abdominal lymph  
 nodes for a duration of 95 wk. Minor responses were observed in  
 three patients. These results suggest that mouse antiidiotypic  
**MAB** that bear the internal image of HMW-MAA may be useful  
 reagents to implement active specific **immunotherapy** in  
 patients with melanoma.

L31 ANSWER 19 OF 28 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD  
 AN 89-05127 BIOTECHDS  
 TI **Immunotoxin therapies** using ricin-A chain;  
 and mouse or human **monoclonal** antibody  
 PA Xoma  
 PI WO 8900583 26 Jan 1989  
 AI WO 88-US2343 12 Jul 1988  
 PRAI US 87-74824 17 Jul 1987  
 DT Patent  
 LA English  
 OS WPI: 89-054070 [07]  
 AN 89-05127 BIOTECHDS  
 AB A new method for **inhibiting** the expansion or activity of  
 a predetermined cell population in a patient involves

Searcher : Shears 308-4994

administering an effective dose of an immunotoxin preparation comprising a binding component capable of attaching to cells and a ricin-A chain (RTA) complexed with the binding component. The RTA contains at least 75%, preferably 85-95% RTA-30. The RTA-30 species (mol.wt. 30,000) may be purified from ricin with an immunoaffinity column. The binding component is an immunoglobulin, preferably a monoclonal antibody (mAb). Intact immunoglobulins or their fragments such as Fv, Fab, F(ab)2, half antibody molecules are used. The preferred IgM or IgG mAbs are of mouse, human or other mammalian origin. Common sources of mAbs are immortalized mouse or human cell lines that may be cloned and screened in accordance with conventional techniques. The new therapy is directed against immune cells, specifically tumor cells or cells from a bone marrow transplant donor. The RTA-30-based immunotoxins can be used to selectively remove harmful cell populations in vivo or extracorporeally with minimal non-specific toxicity. (33pp)

L31 ANSWER 20 OF 28 MEDLINE  
 AN 89275057 MEDLINE  
 DN 89275057  
 TI Cytotoxicity against human tumor cells mediated by the conjugate of anti-epidermal growth factor receptor monoclonal antibody to recombinant ricin A chain.  
 AU Masui H; Kamrath H; Apell G; Houston L L; Mendelsohn J  
 CS Memorial Sloan-Kettering Cancer Center, New York, New York 10021.  
 NC CA37641 (NCI)  
 CA42060 (NCI)  
 SO CANCER RESEARCH, (1989 Jul 1) 49 (13) 3482-8.  
 Journal code: CNF. ISSN: 0008-5472.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 EM 198909  
 AB We have produced monoclonal antibodies against the epidermal growth factor (EGF) receptor which bind to the receptor with high affinity, compete with EGF for binding, block EGF-induced tyrosine kinase activity, and activate internalization and down-regulation of the receptor. These antibodies are cytostatic against cultured A431 cells at concentrations of 5-20 nM. In addition, they prevent the growth of A431 tumor xenografts in athymic mice. In the present experiments, we have attempted to improve the antitumor activity of monoclonal antibody 528 IgG2a against the EGF receptor by linking it to recombinant ricin A chain (rRA). The immunoconjugate (528 IgG-rRA) showed a potent cytotoxic effect on A431 cells in vitro. At a concentration of 10 pM, it inhibited the proliferation of cultured A431

Searcher : Shears 308-4994

cells by 50% and also inhibited protein synthesis in these cells by 50%. Proliferation was prevented and cell death occurred at 528 IgG-rRA concentrations of 60 pM or greater. Recombinant free ricin A chain was far less toxic. The cytotoxic effect of the immunoconjugate was neutralized by 528 IgG at concentrations 100-fold higher than 528 IgG-rRA. When the cytotoxic effect of 528 IgG-rRA was compared among several human cell lines expressing different numbers of EGF receptors, the capacity to inhibit both proliferation and protein synthesis generally correlated with the number of EGF receptors on the plasma membranes of these cells. Since 528 IgG-rRA is a very potent immunotoxin against A431 cells in culture, we designed experiments to test its in vivo antitumor activity against A431 xenografts in athymic mice. To measure the clearance of 528 IgG-rRA, 50 micrograms of immunotoxin were injected i.p. into athymic mice, blood was collected from the animals at regular intervals, and the level of immunotoxin in the serum was assayed by protein synthesis inhibition in cultured A431 cells. The blood level of active immunoconjugate reached a maximum 6 h after i.p. injection. The half-life of the absorption phase was 2.2 h, the half-life for elimination was 9.2 h, and blood levels which could be potentially cytotoxic were maintained for 48-72 h. We investigated a number of immunotoxin treatment schedules, including every other day for 4 days, based on these data. The results demonstrate that, while 528 IgG-rRA has higher in vivo antitumor activity than 528 IgG against A431 cell xenografts, this is accompanied by toxicity against the murine host.

L31 ANSWER 21 OF 28 MEDLINE DUPLICATE 9  
 AN 88210325 MEDLINE  
 DN 88210325  
 TI Radioimmunotherapy of human colonic cancer xenografts with 90Y labeled monoclonal antibodies to carcinoembryonic antigen [published erratum appears in Cancer Res 1988 Aug 15;48(16):4716].  
 AU Sharkey R M; Kaltovich F A; Shih L B; Fand I; Govelitz G; Goldenberg D M  
 CS Center for Molecular Medicine and Immunology, Newark, New Jersey 07103.  
 NC CA 37218 (NCI)  
 CA 43455 (NCI)  
 CA 39841 (NCI)  
 SO CANCER RESEARCH, (1988 Jun 1) 48 (11) 3270-5.  
 Journal code: CNF. ISSN: 0008-5472.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 EM 198808

Searcher : Shears 308-4994

AB **Monoclonal antibodies (MAbs)** to carcinoembryonic antigen (CEA) or alpha-fetoprotein (AFP) were conjugated with diethylenetriaminepentaacetic acid and radiolabeled with 90Y at a specific activity of 4.0-6.0 mCi/mg. Approximately 50% of the radiolabeled anti-CEA antibody (90Y-labeled NP-2) bound to an immunoadsorbent containing CEA while analysis by high performance liquid chromatography revealed that 95-98% of the 90Y was associated with **immunoglobulin**. Less than 5% of the 90Y dissociated from either **MAB** after incubation in plasma for 48 h at 37 degrees C. After injection into nude mice, 98% of the circulating radioactivity remained associated with antibody and no loss of immunoreactivity was observed at 3 days. To evaluate 90Y-labeled NP-2 as a therapeutic agent, varied doses (10-100 microCi) were **administered** as a single i.v. injection into groups of nude mice bearing s.c. implants (0.3-0.4 g) of a CEA-producing human colonic cancer xenograft, GW-39. At the 10-microCi dose, no **inhibition** of tumor growth was observed. After 28 days, tumor growth was **inhibited** by as much as 77% in mice treated with 50 microCi of 90Y-labeled NP-2 as compared to tumor growth in control animals given 90Y-labeled anti-AFP. Doses higher than 50 microCi (75 and 100 microCi) were **toxic** to most of the animals, killing them within 2-3 weeks after **administration**. Marked suppression of circulating leukocytes was observed with 20 and 50 microCi by 1-2 weeks postinjection, but they returned to normal levels 3-4 weeks later. These studies show that treatment with 90Y-labeled **MAbs** against CEA can produce significant antitumor effects. However, **toxicity** to the bone marrow may limit the therapeutic efficacy of systemically **administered** 90Y-labeled **MAbs**.

L31 ANSWER 22 OF 28 MEDLINE DUPLICATE 10  
 AN 88012025 MEDLINE  
 DN 88012025  
 TI Biodistribution of antibodies after intraperitoneal or intravenous injection and effect of carbohydrate modifications.  
 AU Mattes M J  
 CS Center for Molecular Medicine and Immunology, Newark, NJ 07103..  
 SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1987 Oct) 79 (4) 855-63.  
 Journal code: J9J. ISSN: 0027-8874.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 EM 198801  
 AB These studies were designed to improve the strategy for intraperitoneal **immunotherapy** of human ovarian carcinoma with **monoclonal antibodies (MAbs)**. Since ovarian tumor cells generally appear to be confined to the peritoneal cavity, regional therapy is appropriate and can reduce the need for  
 Searcher : Shears 308-4994

strictly tumor-specific **MABs**. In normal mice, with the use of radioiodine-labeled **MABs**, transfer from peritoneal cavity to blood was found to be very rapid, within hours, and this transfer was delayed slightly by increasing the volume injected. The presence of ascitic fluid in mice greatly delayed the rate of transfer. For reduction of possible toxicity for normal cells outside the peritoneal cavity, the hepatic receptor for desialylated serum glycoproteins was used. Neuraminidase treatment of all major mouse **immunoglobulin** classes and subclasses, including **IgM**, **IgG1**, **IgG2a**, **IgG2b**, **IgG3**, and **IgA**, did not cause their rapid blood clearance, although similar treatment of fetuin was effective. Conjugation of **IgG** with galactose, with use of the cyanomethyl derivative, did result in very rapid blood clearance via the hepatic lectin; within 3 minutes clearance was essentially complete. The specificity of uptake was demonstrated by inhibition with desialylated fetuin. Degradation within the liver, release of the radioiodine, and excretion from the animal were also quite rapid, within hours. This conjugation procedure had no effect on the antibody activity of the two **MABs** tested. Such modified **MABs**, therefore, are degraded almost immediately after entering the blood and would be advantageous in intraperitoneal therapy and in other situations in which regional **immunotherapy** is appropriate.

L31 ANSWER 23 OF 28 MEDLINE DUPLICATE 11  
 AN 87102608 MEDLINE  
 DN 87102608  
 TI Effects of **monoclonal** antibodies that block transferrin receptor function on the in vivo growth of a syngeneic murine leukemia.  
 AU Sauvage C A; Mendelsohn J C; Lesley J F; Trowbridge I S  
 NC CA-34787 (NCI)  
 CA-37641 (NCI)  
 CA-25893 (NCI)  
 SO CANCER RESEARCH, (1987 Feb 1) 47 (3) 747-53.  
 Journal code: CNF. ISSN: 0008-5472.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 EM 198705  
 AB The ability of **monoclonal** antibodies (**MABs**) against the murine transferrin receptor to inhibit the growth of transplanted syngeneic AKR/J SL-2 leukemic cells has been investigated. Two rat **IgM** antibodies, RI7 208 and REM 17.2, which both block transferrin receptor function, inhibited the growth of SL-2 leukemic cells in vitro at concentrations of 5-10 micrograms per ml. However, RI7 208 was more effective than REM 17.2 in prolonging survival of tumor-bearing

Searcher : Shears 308-4994



mice. The antitumor effects of RI7 208 MAb were dependent on both the antibody dose and number of leukemic cells inoculated. The serum clearance of [75Se]methionine-labeled RI7 208 and REM 17.2 antibodies was similar and consisted of an initial rapid phase over the first 2 days followed by a slower phase. A single dose of 2 mg of antibody maintained a serum MAb concentration (greater than 10 micrograms/ml) sufficient to inhibit SL-2 leukemic cell growth in vitro for 2-3 days. The liver, kidney, and spleen were the major sites at which each of the antibodies accumulated regardless of whether trace or saturating amounts of antibody were administered. The specific activity of antibody found in s.c. SL-2 tumors was about 2-fold less than that of liver. It was shown that multiple doses of RI7 208 MAb administered on a schedule aimed at maintaining a therapeutic serum level of MAb for 1-3 weeks were more effective than a single dose. Further, administration of RI7 208 MAb, in combination with the anti-Thy-1.1 MAb 19E12, was more effective than either antibody alone. SL-2 mutant cells were selected that were resistant to growth inhibitory effects of RI7 208 in vitro. The effects of RI7 208 MAb on the growth of these mutant cells in vivo suggests the major mechanism by which the MAb inhibits SL-2 tumor growth is by directly blocking receptor function. Acute toxicity associated with administration of the MAb was minimal. However, assays of myeloid and erythroid colony-forming units in bone marrow and spleen of mice given multiple doses of RI7 208 showed a depression of stem cell activity in bone marrow and elevated numbers of erythroid and cellular colony-forming units in the spleen.

L31 ANSWER 24 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE  
12

AN 85061095 EMBASE

TI Human anti-murine immunoglobulin responses in patients receiving  
monoclonal antibody therapy.

AU Schroff R.W.; Foon K.A.; Beatty S.M.; et al.

CS Biological Therapeutics Branch, Biological Response Modifiers  
Program, National Cancer Institute, Frederick, MD 21701, United  
States

SO CANCER RES., (1985) 45/2 (879-885).

CODEN: CNREA8

CY United States

LA English

AB Human anti-murine immunoglobulin responses were assessed  
in serum from three groups of patients receiving murine  
monoclonal antibody therapy. Each of the three patient  
groups responded differently. Chronic lymphocytic leukemia patients  
demonstrated little or no preexisting murine immunoglobulin  
G-reactive antiglobulin prior to treatment, while the cutaneous

Searcher : Shears 308-4994

T-cell lymphoma and melanoma patients demonstrated preexisting antiglobulin levels in the same range as those demonstrated in healthy controls. None of 11 chronic lymphocytic leukemia patients receiving the T101 **monoclonal** antibody demonstrated an antiglobulin response, whereas all four of the cutaneous T-cell lymphoma patients receiving the same antibody developed increased levels of antiglobulins. Three of nine malignant melanoma patients receiving the 9.2.27 **monoclonal** antibody showed an increase in antiglobulin titers. In patients developing antiglobulin responses, the response was rapid, typically being detectable within 2 weeks. The antiglobulins were primarily **immunoglobulin G** and, with the exception of a single melanoma patient in whom the response appeared to have a substantial 9.2.27-specific component (i.e., antidiotype), were cross-reactive with most murine **immunoglobulin G** preparations tested. This pattern of results suggested that the antiglobulin was a secondary immune reaction with elevation of the levels of preexisting antiglobulin which was cross-reactive with the mouse antibody **administered**. While the presence of serum antiglobulin would be expected to present major complications to **monoclonal** antibody therapy, no clinical **toxicity** related to antiglobulin responses was observed in these patients, and no **inhibition** of antibody localization on tumor cells was seen.

L31 ANSWER 25 OF 28 CANCERLIT  
 AN 83608558 CANCERLIT  
 DN 83608558  
 TI **MONOCLONAL** ANTIBODY AND AN ANTIBODY-TOXIN CONJUGATE TO A CELL SURFACE PROTEOGLYCAN OF MELANOMA CELLS SUPPRESS IN VIVO TUMOR GROWTH.  
 AU Bumol T F; Wang Q C; Reisfeld R A; Kaplan N O  
 CS Dept. Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037.  
 SO Proc Natl Acad Sci U S A, (1983). Vol. 80, No. 2, pp. 529-533. ISSN: 0027-8424.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS ICDB  
 LA English  
 EM 198304  
 AB A **monoclonal** antibody directed against a cell surface chondroitin sulfate proteoglycan of human melanoma cells, 9.2.27, and its diphtheria toxin A chain (DTA) conjugate were investigated for their effects on in vitro protein synthesis and in vivo tumor growth of human melanoma cells. The 9.2.27 IgG and its DTA conjugate display similar serological activities against melanoma target cells but only the conjugate can induce consistent in vitro **inhibition** of protein synthesis and **toxicity** in M21 melanoma cells. However, both 9.2.27 IgG and its DTA conjugate effects significant suppression of M21 tumor growth in  
 Searcher : Shears 308-4994

vivo in an **immunotherapy** model of a rapidly growing tumor in athymic nu/nu mice, suggesting that other host mechanisms may mediate **monoclonal** antibody-induced tumor suppression.  
(Author abstract) (28 Refs)

L31 ANSWER 26 OF 28 MEDLINE DUPLICATE 13  
AN 84106469 MEDLINE  
DN 84106469  
TI Ricin A-chain conjugated with **monoclonal** anti-L1210 antibody. In vitro and in vivo antitumor activity.  
AU Kishida K; Masuho Y; Saito M; Hara T; Fuji H  
NC CA26479 (NCI)  
SO CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1983) 16 (2) 93-7.  
Journal code: CN3. ISSN: 0340-7004.  
CY GERMANY, WEST: Germany, Federal Republic of  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 198405  
AB In studies of antitumor antibody-cytotoxic agent conjugates as potential antitumor agents with improved tumor specificity, the **toxic** subunit A-chain of ricin was conjugated with a **monoclonal** antibody to a tumor-associated antigen expressed weakly on murine leukemia L1210 cells and strongly on L1210/GZL cells, a guanazole-resistant subline of L1210, employing N-succinimidyl 3-(2-pyridyldithio)propionate as cross-linking agent. The conjugate (anti-L1210 conjugate) exhibited a potent concentration-dependent cytotoxicity against cultured L1210/GZL cells, and **inhibited** cell growth at concentrations over 0.8 micrograms/ml. The conjugate killed all L1210/GZL cells at a concentration of 100 micrograms/ml. Neither nonimmune conjugate similarly prepared from mouse nonimmune IgG nor unconjugated anti-L1210 IgG alone showed cytotoxicity against L1210/GZL cells. When (BALB/c X DBA/2)F1 mice inoculated with  $1 \times 10^5$  L1210/GZL cells were treated with IP injections of 27 micrograms anti-L1210 conjugate 1 h and 5 days after tumor cell inoculation, a life-prolonging effect was observed. [Lifespan in treated animals as percentage of that in controls (T/C) = 146%]. However, when the dose per injection was increased to 50 micrograms per mouse, survival was the same as in the control group. Postmortem examination of mice that had been treated with 50 micrograms anti-L1210 conjugate revealed lesions with necrosis and hemorrhage in the liver parenchyma and the intestinal epithelium, respectively. A similar **toxic** effect on the host mice was also observed with nonimmune conjugate.

L31 ANSWER 27 OF 28 CANCERLIT  
AN 82614600 CANCERLIT  
DN 82614600

Searcher : Shears 308-4994

TI SPECIFIC KILLING OF HUMAN AND MOUSE TUMOR CELLS BY IMMUNOTOXINS.  
 AU Casellas P; Blythman H E; Brown J P; Gros O; Gros P; Hellstrom K E;  
 Hellstrom I; Jansen F K; Poncelet P; Vidal H  
 CS Centre de Recherches CLIN MIDY, Montpellier, France.  
 SO Protides Biol Fluid Proc Colloq, (1982). Vol. 29, pp. 927-932.  
 DT (MEETING PAPER)  
 FS ICDB  
 LA English  
 EM 198206  
 AB **Monoclonal** antibodies (anti-Thy 1.2 and anti-human melanoma P97) were used to replace the binding moiety of the B-chain of ricin, in order to obtain immunotoxins that use the purified A-chain of ricin as the **toxic** moiety. The A-chain was coupled to the antibodies via a disulfide linkage, allowing a linkage of active A-chain to antibody ratio of 3:1 for IgM anti-Thy 1.2 and 1.4:1 for the IgG anti-melanoma immunotoxin. Both immunotoxins showed specific cytotoxicity for their respective target cells. In vitro tests of protein synthesis **inhibition** and of **inhibition** of colony formation demonstrated the specific activity of the immunotoxins. Both immunotoxins could specifically kill the last target cell without damaging control cells, and a specific killing index could be calculated. The loss of binding capacity due to conjugation was estimated to be 10% for anti-Thy 1.2 immunotoxin and 30% for anti-melanoma immunotoxin. (11 Refs)

L31 ANSWER 28 OF 28 CANCERLIT  
 AN 83601990 CANCERLIT  
 DN 83601990  
 TI **MONOCLONAL ANTI-MM46 ANTIBODY:RICIN A CHAIN CONJUGATE: IN VITRO AND IN VIVO ANTITUMOR ACTIVITY.**  
 AU Seto M; Umemoto N; Saito M; Masuho Y; Hara T; Takahashi T  
 CS (c/o Hara), Teijin Inst. Biomedical Res., Asahigaoka, Hino, Tokyo 191, Japan.  
 SO Cancer Res, (1982). Vol. 42, No. 12, pp. 5209-5215.  
 ISSN: 0008-5472.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS ICDB  
 LA English  
 EM 198302  
 AB In an approach to antitumor agents with improved tumor specificity, the ricin **toxic** subunit A chain was covalently coupled with a **monoclonal** IgG2b antibody directed against MM antigen, a tumor-specific antigen on syngeneic mouse mammary tumor MM46 cells (anti-MM46 IgG), using N-succinimidyl 3-(2-pyridyldithio)propionate as cross-linking agent. The conjugate thus prepared (anti-MM46 conjugate) showed potent dose-dependent cytotoxicity against MM antigen-positive MM46 cells in vitro and **inhibited** the cell growth at concentrations above 1 ug/ml.

Searcher : Shears 308-4994

The immunological specificity was verified by the observation that anti-MM46 conjugate did not show cytotoxicity against MM antigen-negative MM48 cells. Neither nonimmune conjugate similarly prepared from mouse nonimmune IgG nor unconjugated anti-MM46 IgG alone exhibited cytotoxicity against MM46 cells. Anti-MM46 IgG still retained considerable in vitro complement-dependent cytotoxicity against MM46 cells after conjugation with ricin A chain. In Winn-type tumor-neutralizing assay in which C3H/He mice were inoculated ip or sc with MM46 cells preincubated with a test material, anti-MM46 conjugate showed greater activity than did anti-MM46 IgG. A markedly enhanced efficacy of anti-MM46 conjugate was also observed in therapeutic experiments. When a group of five C3H/He mice inoculated ip with  $5 \times 10^4$  MM46 cells were treated with an ip injection of 1 ug of anti-MM46 conjugate on Days 1, 3, and 5, all five mice survived tumor free. The in vivo efficacy of anti-MM46 conjugate over anti-MM46 IgG alone was demonstrated by therapeutic experiments as well as by tumor-neutralizing assays. Although anti-MM46 conjugate showed no antitumor effect when injected ip to C3H/He mice bearing sc-inoculated MM46 tumor on Days 1, 3, 5, and 7 at a dose of 10 ug, it inhibited tumor growth when injected intraregionally to tumor-bearing mice, suggesting that the conjugate is effective also to solid-type MM46 tumor if a sufficient amount of anti-MM46 conjugate reaches the tumor site. (26 Refs)

=> d his 132-

(FILE 'CAPLUS, BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGLAUNCH, DRUGB, CANCERLIT, USPATFULL' ENTERED AT 17:12:49 ON 07 DEC 1998)

-Author (S)

L32 121 S ROSOK M?/AU  
 L33 326 S YELTON D?/AU  
 L34 33 S L32 AND L33  
 L35 101 S (L32 OR L33) AND L11  
 L36 112 S L34 OR L35  
 L37 11 S L35 AND TOXIC?  
 L38 39 S L34 OR L37  
 L39 15 DUP REM L38 (24 DUPLICATES REMOVED)

=> d 1-15 bib abs

L39 ANSWER 1 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1  
 AN 1998:112463 CAPLUS  
 DN 128:204075  
 TI A method for inhibiting immunoglobulin-induced toxicity resulting from the use of immunoglobulins in therapy and in vivo diagnosis  
 Searcher : Shears 308-4994

08/905293

IN Rosok, Mae Joanne; Yelton, Dale E.

PA Bristol-Myers Squibb Co., USA

SO PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805787	A1	19980212	WO 97-US13562	19970801
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9739688	A1	19980225	AU 97-39688	19970801
PRAI	US 96-23033		19960802		
	WO 97-US13562		19970801		

AB The present invention provides a method for inhibiting Ig -induced toxicity resulting from immunotherapy in a subject comprising administering an Ig or Ig fusion protein mol. to the subject, the Ig mol. having a variable region and a const. region, the Ig mol. being modified prior to administration by inactivation of at least a portion of the const. region. The Ig. fusion protein is a IgG, IgM, or IgA which recognizes and binds Ley or Le. The Ig. fusion protein may also be labeled with radiolabel, enzyme, chromophore, chemiluminescer or fluorescer for tumor diagnosis, or conjugates to cytotoxic agent for cancer therapy. HBR96-2B, hBR96-2C, hBR96-2D, hBR96-2E, hBR96-2F, hBR96-2G, and hBR96-2H are provided for the diagnosis and therapy purposes.

L39 ANSWER 2 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 2

AN 1998:545386 CAPLUS

DN 129:188362

TI Mutant BR96 antibodies reactive with human carcinomas

IN Yelton, Dale; Glaser, Scott; Huse, William; Rosok, Mae Joanne

PA Bristol-Myers Squibb Co., USA

SO U.S., 71 pp. Cont.-in-part of U. S. Ser. No. 285,936.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5792456	A	19980811	US 95-487860	19950607
	US 5728821	A	19980317	US 94-285936	19940804
	CA 2155397	AA	19960205	CA 95-2155397	19950803
	AU 9528349	A1	19960215	AU 95-28349	19950803

Searcher : Shears 308-4994

08/905293

EP 699756                    A1    19960306                    EP 95-305444                    19950803  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,  
PT, SE  
JP 08191692                    A2    19960730                    JP 95-230629                    19950804  
PRAI US 94-285936                    19940804  
US 95-487860                    19950607  
OS    MARPAT 129:188362  
AB    The authors disclose the prepn. and improved reactivity of  
polypeptide muteins of the BR96 antibody directed to the Lewis Y  
determinant. Muteins were constructed using codon mutagenesis of  
heavy chain CDRs. Application of mutein immunoconjugates in cancer  
diagnosis and treatment is discussed.

L39    ANSWER 3 OF 15    USPATFULL  
AN    1998:28198    USPATFULL  
TI    Mutant BR96 antibodies reactive with human carcinomas  
IN    **Yelton, Dale**, Seattle, WA, United States  
Glaser, Scott, San Diego, CA, United States  
Huse, William, Del Mar, CA, United States  
**Rosok, Mae Joanne**, Seattle, WA, United States  
PA    Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S.  
corporation)  
PI    US 5728821    980317  
AI    US 94-285936    940804 (8)  
DT    Utility  
EXNAM    Primary Examiner: Feisee, Lila; Assistant Examiner: Ungar, Susan  
LREP    Merchant, Gould, Smith, Edell, Welter & Schmidt  
CLMN    Number of Claims: 21  
ECL    Exemplary Claim: 1,4  
DRWN    25 Drawing Figure(s); 23 Drawing Page(s)  
LN.CNT 3197  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB    The present invention provides mutant BR96 polypeptides (and  
nucleotide sequences encoding them) having a variable region  
comprising an amino acid sequence derived from the variable region  
of BR96.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39    ANSWER 4 OF 15    CAPLUS    COPYRIGHT 1998 ACS                    DUPLICATE 3  
AN    1998:134102    CAPLUS  
DN    128:256176  
TI    Analysis of BR96 binding sites for antigen and anti-idiotypic by  
codon-based scanning mutagenesis  
AU    **Rosok, Mae Joanne**; Eghtedarzadeh-Kondri, Mohammad; Young,  
Kelly; Bajorath, Jurgen; Glaser, Scott; **Yelton, Dale**  
CS    Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA,  
98121, USA  
SO    J. Immunol. (1998), 160(5), 2353-2359  
Searcher : Shears    308-4994

CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB We performed a scanning mutagenesis study of heavy chain complementarity-detg. region (CDR) residues to identify how mutations affected binding of the anti-carcinoma mAb BR96 to Ag, Lewis Y, and to an anti-Id Ab (anti-Id). By ELISA, we demonstrated that the anti-Id bound close to the Ag binding site of BR96, but the anti-Id and Ag sites were not identical. Immunoblot anal. and screening of light and heavy chain CDR libraries with multiple mutations in each CDR suggested that the heavy chain had greater involvement in anti-Id binding. We then analyzed contributions of individual residues in the heavy chain CDRs to binding of Ag and anti-Id. In as filamentous phage vector contg. BR96 V region sequences, mutations were introduced by codon-based mutagenesis at single positions within the three heavy chain CDRs. The resulting libraries of Fab fragments had all amino acids represented at a CDR position. We evaluated the expressed Fabs for binding to Ag and anti-Id by plaque lift assay. We identified the positions with mutations that had the greatest neg. effect on binding to the anti-Id and to Ag and analyzed them on the basis of the BR96 x-ray structure. The residues most important for binding to the anti-Id were located in heavy chain CDR1 and CDR2 and were peripheral to the residues within the Lewis Y binding pocket.

L39 ANSWER 5 OF 15 USPATFULL

AN 97:78179 USPATFULL

TI Monoclonal antibody compositions cross-reactive and cross-protective against *P. aeruginosa* serotypes

IN Siadak, Anthony W., Seattle, WA, United States

Rosok, Mae J., Seattle, WA, United States

PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)

PI US 5662905 970902

AI US 94-366204 941229 (8)

RLI Continuation of Ser. No. US 93-66604, filed on 24 May 1993, now patented, Pat. No. US 5378812 which is a continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807394, filed on 10 Dec 1985, now abandoned.

DT Utility

EXNAM Primary Examiner: Loring, Susan A.

LREP Townsend And Townsend And Crew LLP

CLMN Number of Claims: 8

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1412

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Searcher : Shears 308-4994



AB Cell lines have been produced that secrete human monoclonal antibodies capable of binding to the lipopolysaccharide molecules of selected *Pseudomonas aeruginosa* IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included. Prior to filing of this patent application the continuous transformed human cell lines 1C1, 6D6 and 8H7 described herein were deposited in the American Type Culture Collection and given the designations CRL 8941, 9171, and 9258, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 6 OF 15 USPATFULL

AN 97:40481 USPATFULL

TI Method for inhibiting the viability of *Pseudomonas aeruginosa* with cross-reactive and cross-protective monoclonal antibodies

IN Siadak, Anthony W., Seattle, WA, United States

Rosok, Mae J., Seattle, WA, United States

PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)

PI US 5628996 970513

AI US 95-463910 950605 (8)

RLI Division of Ser. No. US 94-366204, filed on 29 Dec 1994 which is a continuation of Ser. No. US 93-66604, filed on 24 May 1993, now patented, Pat. No. US 5378812 which is a continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807394, filed on 10 Dec 1985, now abandoned

DT Utility

EXNAM Primary Examiner: Housel, James C.; Assistant Examiner: Loring, Susan A.

LREP Townsend and Townsend and Crew LLP

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1405

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cell lines have been produced that secrete human monoclonal antibodies capable of binding to the lipopolysaccharide molecules of selected *Pseudomonas aeruginosa* IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 7 OF 15 USPATFULL

AN 97:38410 USPATFULL

TI Monoclonal antibodies cross-reactive and cross-protective against human monoclonal antibodies against pseudomonas aeruginosa serotypes

IN Siadak, Anthony W., Seattle, WA, United States

Rosok, Mae J., Seattle, WA, United States

PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)

PI US 5627067 970506

AI US 95-462370 950605 (8)

RLI Division of Ser. No. US 94-366204, filed on 29 Dec 1994 which is a continuation of Ser. No. US 93-66604, filed on 24 May 1993, now patented, Pat. No. US 5378812 which is a continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807394, filed on 10 Dec 1985, now abandoned

DT Utility

EXNAM Primary Examiner: Loring, Susan A.

LREP Townsend and Townsend and Crew

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1391

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cell lines have been produced that secrete human monoclonal antibodies capable of binding to the lipopolysaccharide molecules of selected Pseudomonas aeruginosa IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included.

Prior to filing of this patent application the continuous transformed human cell lines 1C1, 6D6, and 8H7 described herein were deposited in the American Type Culture Collection and given the designations CRL 8941, 9171, and 9258, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 8 OF 15 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD

AN 96-05132 BIOTECHDS

TI New mutant BR96 polypeptides;

monoclonal antibody and chimeric antibody engineering; protein engineering for increased affinity for Lewis-Y tumor-associated antigen; use in cancer diagnosis and therapy

Searcher : Shears 308-4994

08/905293

AU Yelton D; Glaser S; Huse W; Rosok M J  
PA Bristol-Squibb  
LO New York, NY, USA.  
PI AU 9528349 15 Feb 1996  
AI AU 95-28349 3 Aug 1995  
PRAI US 95-487860 7 Jun 1995; US 94-285936 4 Aug 1994  
DT Patent  
LA English  
OS WPI: 96-129723 [14]  
AN 96-05132 BIOTECHDS  
AB A new mutant BR96 protein contains a protein sequence including specified sequences in a complementarity determining region (CDR), heavy chain variable region and more specifically CDR1, CDR2 and CDR3. The protein may be a monoclonal antibody, chimeric antibody, Fab, F(ab')<sub>2</sub> or Fv fragment. DNA encoding the protein (e.g. cDNA) may be inserted in a plasmid vector for expression in a host cell, e.g. Escherichia coli or a eukaryote. The mutant BR96 antibody may be produced by mutagenesis of DNA encoding BR96 and purification from a recombinant host. The mutant BR96 antibody has an increased affinity for the Lewis-Y antigen, which is expressed by carcinomas and some different epithelial cells, as compared to native BR96. The antibody may be used in cancer diagnosis, or in production of conjugate immunotoxins with cytostatic activity against cancer or proliferative disease. (108pp)

L39 ANSWER 9 OF 15 CAPLUS COPYRIGHT 1998 ACS

AN 1996:222491 CAPLUS

DN 124:250918

TI Novel mutant BR96 monoclonal antibodies, their production using plasmids, and their application as immunoconjugates with cytotoxic agents in human carcinoma treatment

IN Yelton, Dale; Glaser, Scott; Huse, William; Rosok, Mae Joanne

PA Bristol-Myers Squibb Company, USA

SO Eur. Pat. Appl., 91 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	EP 699756	A1	19960306	EP 95-305444	19950803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5728821	A	19980317	US 94-285936	19940804
	US 5792456	A	19980811	US 95-487860	19950607
PRAI	US 94-285936		19940804		
	US 95-487860		19950607		

AB The present invention provides mutant BR96 polypeptides (and cDNAs  
Searcher : Shears 308-4994

encoding them) having a variable region comprising an amino acid sequence substantially homologous to the variable region of monoclonal antibody BR96. Immunoconjugates, BR96 mutants conjugated with cytotoxic agents have applications in treatments of human carcinomas.

L39 ANSWER 10 OF 15 TOXLIT  
 AN 1996:76175 TOXLIT  
 DN CA-124-250918S  
 TI Novel mutant BR96 monoclonal antibodies, their production using plasmids, and their application as immunoconjugates with cytotoxic agents in human carcinoma treatment.  
 AU Yelton D; Glaser S; Huse W; Rosok MJ  
 SO (1996). Eur. Pat. Appl. PATENT NO. 699756 03/06/96 (Bristol-Myers Squibb Company).  
 CY United States  
 DT Patent  
 FS CA  
 LA English  
 OS CA 124:250918  
 EM 199605  
 AB The present invention provides mutant BR96 polypeptides (and cDNAs encoding them) having a variable region comprising an amino acid sequence substantially homologous to the variable region of monoclonal antibody BR96. Immunoconjugates, BR96 mutants conjugated with cytotoxic agents have applications in treatments of human carcinomas.

L39 ANSWER 11 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 5  
 AN 1996:572221 CAPLUS  
 DN 125:218995  
 TI A combinatorial library strategy for the rapid humanization of anticarcinoma BR96 Fab  
 AU Rosok, Mae Joanne; Yelton, Dale E.; Harris, Linda J.; Bajorath, Jurgen; Hellstrom, Karl-Erik; Hellstrom, Ingegerd; Cruz, Gina A.; Kristensson, Karin; Lin, Huey; et al.  
 CS Bristol-Myers Squibb Pharmaceutical Res. Inst., Seattle, WA, 98121, USA  
 SO J. Biol. Chem. (1996), 271(37), 22611-22618  
 CODEN: JBCHA3; ISSN: 0021-9258  
 DT Journal  
 LA English  
 AB The authors have used a combinatorial mutagenesis strategy to humanize BR96, a monoclonal antibody that binds to the Lewis Y class of tumor antigens. This approach allows simultaneous assessment of hundreds of humanized variable regions to identify the mols. that best preserve affinity, thus overcoming the major drawback of current humanization procedures, the requirement to construct and analyze each humanized antibody sep. Murine residues of BR96 were

Searcher : Shears 308-4994

mutated to human if they were solvent-exposed residues that did not participate in the formation of the antigen binding site and were not at the interface of the light and heavy chain. At positions that might be involved in binding to antigen, the choice between the murine and human residue was more difficult. Murine and human alternatives were incorporated into a combinatorial library at positions representing buried residues that might affect the structural integrity of the antigen binding site. By encoding this library of humanized BR96 Fabs in an M13 phage vector, the authors rapidly identified several candidates with nearly identical antigen binding, within 2-fold, of the chimeric Fab. Addnl. mutagenesis directed at sites suggested in the literature as potentially important for antigen binding in a similar anti-Lewis Y antibody yielded no further improvements.

L39 ANSWER 12 OF 15 USPATFULL

AN 95:1714 USPATFULL

TI Monoclonal antibodies cross-reactive and cross-protective against *P. aeruginosa* serotypes

IN Siadak, Anthony W., Seattle, WA, United States

Rosok, Mae J., Seattle, WA, United States

PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)

PI US 5378812 950103

AI US 93-66604 930524 (8)

RLI Continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807391, filed on 10 Dec 1985, now abandoned

DT Utility

EXNAM Primary Examiner: Lacey, David L.; Assistant Examiner: Loring, Susan A.

LREP Townsend and Townsend Khourie and Crew

CLMN Number of Claims: 6

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1363

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cell lines have been produced that secrete human monoclonal antibodies capable of binding to the lipopolysaccharide molecules of selected *Pseudomonas aeruginosa* IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included.

Prior to filing of this patent application the continuous transformed human cell lines 1C1, 6D6, and 8H7 described herein were deposited in the American Type Culture Collection and given

Searcher : Shears 308-4994

the designations CRL 8941, 9171, and. 9258, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 13 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 6  
 AN 1995:740198 CAPLUS  
 DN 123:141273  
 TI Affinity maturation of the BR96 anti-carcinoma antibody by  
 codon-based mutagenesis  
 AU Yelton, Dale E.; Rosok, Mae Joanne; Cruz, Gina;  
 Cosand, Wesley L.; Bajorath, Juergen; Hellstroem, Ingegerd;  
 Hellstroem, Karl Erik; Huse, William D.; Glaser, Scott M.  
 CS Bristol-Myers Squibb Pharmaceutical Res. Inst., Seattle, WA, 98121,  
 USA  
 SO J. Immunol. (1995), 155(4), 1994-2004  
 CODEN: JOIMA3; ISSN: 0022-1767  
 DT Journal  
 LA English  
 AB We have increased up to 65-fold the avidity of BR96, a mAb  
 recognizing Lewis Y (Ley)-related Ags expressed on the surface of  
 many human carcinomas. Libraries of mutations in the  
 complementarity-detg. regions (CDRs) of BR96 were constructed in an  
 M13 phage Fab expression vector by codon-based mutagenesis, a method  
 that efficiently introduces large nos. and potentially all  
 combinations of amino acid substitutions. Two mutants that improved  
 the affinity of BR96 to tumor Ag were identified by screening the  
 libraries on carcinoma cell lines. One mutant, M1, at position 97  
 (Asp to Ala) in CDR3 of the heavy chain, resulted in an 8- to  
 10-fold improvement in Ag binding, as assessed by ELISA. A second  
 mutant, M2, at position 53 (Gly to Asp) in CDR2 of VH increased  
 binding three- to fivefold. When these mutations were combined, the  
 resulting Fab M3 was improved approx. 30-fold. An addnl. library  
 was constructed in CDR1 of M1. M4, a mutation with three amino acid  
 substitutions in CDR1, was isolated by screening the library with an  
 enzyme conjugate of synthetic Ley tetrasaccharide (sLey). This  
 mutant improved BR96 Fab affinity to sLey an estd. 15- to 20-fold by  
 ELISA, and 14-fold as measured by surface plasmon resonance. The M4  
 IgG had 65-fold improved avidity to sLey relative to the BR96 IgG.  
 The mutants will be useful for comparison of the efficacy of Abs  
 with different affinities for delivery of cytotoxic agents to tumor  
 cells.

L39 ANSWER 14 OF 15 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD  
 AN 90-48785 DRUGU T S  
 TI Phase I Trial of Chimeric Monoclonal Antibody L6 (ChL6).  
 AU Goodman G E; Murray J L; Hellstrom K E; Nicaise C; Yelton D  
 ; Palazollo P  
 LO Seattle, Washington, Houston, Texas, Wallingford, Connecticut,  
 United States

Searcher : Shears 308-4994

SO Proc.Am.Assoc.Cancer Res. (31, 81 Meet.; 174, 1990) ISSN:  
0197-016X

AV Swedish Hospital Tumor Institute, Seattle, WA, U.S.A. (8 authors).

LA English

DT Journal

FA AB; LA; CT

FS Literature

AN 90-48785 DRUGU T S

AB In a phase I trial of 17 patients with breast, colon, ovary and lung cancers, a single i.v. infusion of a chimeric monoclonal antibody L6 (ChL6), was associated with severe headaches and fever at higher doses. ChL6 remained in the serum and was present on tumor cells for several days. (congress abstract).

ABEX Methods ChL6 was given to 17 patients as a single 4-18 hr i.v. infusion at dose levels of 35, 70, 140, 350 and 700 mg/sq.m.  
Results Patients receiving doses over 140 mg/sq.m developed severe headaches and fever which lasted 12-48 hr. No laboratory evidence of toxicity was observed. Serum complements fell within 24 hr and remained low for 2 wk. ChL6 serum half-life was 4-5 days. Biopsies at 3 days showed localization at doses above 70 mg/sq.m and saturation at 700 mg/sq.m. On day 7, ChL6 was still present on tumor cells. Human anti-mouse antibody was detected in 1 patient. (E61/MB)

## L39 ANSWER 15 OF 15 USPATFULL

AN 89:43140 USPATFULL

TI Monoclonal antibodies to pseudomonas aeruginosa flagella

IN Rosok, Mae J., Seattle, WA, United States  
Lostrom, Mark E., Redmond, WA, United States

PA Genetic Systems Corporation, Seattle, WA, United States (U.S. corporation)

PI US 4834976 890530

AI US 86-946554 861224 (6)

RLI Continuation-in-part of Ser. No. US 86-881984, filed on 3 Jul 1986

DT Utility

EXNAM Primary Examiner: Warden, Robert J.; Assistant Examiner: Wagner, Richard

LREP Townsend and Townsend

CLMN Number of Claims: 22

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1574

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cell lines have been produced that secrete monoclonal antibodies capable of binding to the flagellar proteins of selected Pseudomonas aeruginosa strains. Some of these antibodies have been found to be protective against lethal challenges of P. aeruginosa. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma

Searcher : Shears 308-4994

08/905293

fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections, are included.

Prior to filing this application, the continuous transformed cell lines PaF4 IVE8, FA6 IIG5, 20H11, and 21B8, described herein, were deposited in the America Type Culture Collection and given the designations HB9129, HB9130, CRL 9300, and CRL 9301, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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